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(30) Priority Data: 09/115,453 14 July 1998 (14.07.98) 09/116,134 14 July 1998 (14.07.98) 09/159,822 23 September 1998 (23.09.9 09/159,812 23 September 1998 (23.09.9 09/232,880 15 January 1999 (15.01.99) 09/232,149 15 January 1999 (15.01.99) 09/288,946 9 April 1999 (09.04.99) (71) Applicant: CORIXA CORPORATION [US/US]; S 1124 Columbia Street, Seattle, WA 98104 (US).	(8) (8) (8) (8) (8) (8) (8) (8) (8) (8)	(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
(72) Inventors: DILLON, Davin, Clifford; 21607 N.E. 24 Redmond, WA 98053 (US). HARLOCKER, Susar 6203 20th Avenue N.W., Seattle, WA 98107 (US). Jiang; 5001 South 232nd Street, Kent, WA 98032 (I Jiangchun; 15805 S.E. 43rd Place, Bellevue, W (US). MITCHAM, Jennifer, Lynn; 16677 North Street, Redmond, WA 98052 (US).	ı, Loui YUQ I US). X 'A 980	Se; Published (U, With international search report. (U, U, 06 (88) Date of publication of the international search report:

(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

(57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

INTERNATIONAL SEARCH REPORT

PCT/US 99/15838

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C12N15/12 C07K14/47 A61K39/395 G01N33/68 C12Q1/68 C12N5/02 G01N33/574 CO7K16/30 C12N15/62 //A61P35/00 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) C12N C07K IPC 7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Category ' Relevant to claim No. Α WO 97 33909 A (CORIXA CORP) 1-22,18 September 1997 (1997-09-18) 29-31, 35-49, 53-79 the whole document SJOGREN H O: "Therapeutic immunization 23-28, Α against cancer antigens using genetically 32-34. 53-57 engineered cells" IMMUNOTECHNOLOGY, vol. 3, no. 3, 1 October 1997 (1997-10-01), pages 161-172, XP004097000 ISSN: 1380-2933 the whole document -/--Further documents are listed in the continuation of box C. Patent family members are listed in annex. Special categories of cited documents: T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international "X" document of particular relevance; the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another "Y" document of particular relevance; the claimed invention citation or other special reason (as specified) cannot be considered to involve an inventive step when the document is combined with one or more other such docu-*O* document referring to an oral disclosure, use, exhibition or other means ments, such combination being obvious to a person skilled in the art. *P" document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 0 4. 05. 00 31 January 2000 Authorized officer Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijawijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 ANDRES S.M.

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INTERNATIONAL SEARCH REPORT

International Application No PCT, US 99/15838

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Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Α	CHU R S ET AL: "CPG OLIGODEOXYNUCLEOTIDES ACT AS ADJUVANTS THAT SWITCH ON T HELPER 1 (TH1) IMMUNITY" JOURNAL OF EXPERIMENTAL MEDICINE, vol. 186, no. 10, 1 November 1997 (1997-11-01), pages 1623-1631, XP002910130 ISSN: 0022-1007 the whole document	14-20, 25-27, 41-47
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	page 3, line 20 -page 22, line 2 page 35, line 9 - last line page 76, line 34 -page 78, line 22 claims	
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	page 2 -page 24 example 2 page 35, line 15 -page 36, line 11 page 81, line 14 -page 83, line 11 claims	

INTERNATIONAL SEARCH REPORT

In ational application No.

PCT/US 99/15838

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Remark: Although claims 29-34, 48-49, 52, 55-57 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-79 all partially
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Invention 1. Claims: 1-79 (all partially)

A polypeptide comprising at least an immunogenic portion of a prostate tumor protein defined as SEQ ID 108 and which is encoded by the related SEQ IDs 2,3,107 (according to the Description of the Sequence Identifiers), fragments and variants thereof, fusion proteins comprising it, polynucleotides or oligonucleotides derived therefrom, antibodies or fragments thereof binding to the polypeptide, pharmaceutical compositions or vaccines comprising these products and their use in methods for inhibiting, monitoring or diagnosing the development of a prostate cancer, for removing tumor cells from a sample or for expanding and/or stimulating T-cells.

Inventions 2. to 439. Claims: 1-79 (all partially and as far as applicable)

As for subject 1. but concerning respectively SEQ IDs 1,4-106,109-111,115-171,173-175,177,179-305,307-315,326,328,330,332-335,340-375,381,382 and 384-472.

INTERNATIONAL SEARCH REPORT

mation on patent family members

International Application No PC1, JS 99/15838

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INTERNATIONAL APPLICATION PU	UBLISH	IED U	NDER THE PATENT COOPERATION TREATY (PCT)	
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(DI) International representation	PCT/US9 y 1999 (1		Columbia, 701 Fifth Avenue, Seattle, WA 98104–70	00 192
09/116,134 14 July 1998 (14.07 09/159,822 23 September 1998 09/159,812 23 September 1998 09/232,880 15 January 1999 (15 09/232,149 15 January 1999 (15 09/288,946 9 April 1999 (09.04 (71) Applicant: CORIXA CORPORATION [US 1124 Columbia Street, Seattle, WA 98104 (72) Inventors: DILLON, Davin, Clifford; 21607 Redmond, WA 98053 (US). HARLOCKE 6203 20th Avenue N.W., Scattle, WA 9810 Jiang; 5001 South 232nd Street, Kent, WA Jiangchun; 15805 S.E. 43rd Place, Belle	10) Priority Data: 09/115,453 14 July 1998 (14.07.98) 09/159,822 23 September 1998 (23.09.98) US 09/159,812 23 September 1998 (23.09.98) US 09/232,880 15 January 1999 (15.01.99) US 09/232,149 15 January 1999 (15.01.99) US 09/288,946 9 April 1999 (09.04.99) US 01) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US). 12) Inventors: DILLON, Davin, Clifford; 21607 N.E. 24th Street, Redmond, WA 98053 (US). HARLOCKER, Susan, Louise; 6203 20th Avenue N.W., Scattle, WA 98107 (US). YUQIU, Jiang; 5001 South 232nd Street, Kent, WA 98032 (US). XU, Jiangchun; 15805 S.E. 43rd Place, Bellevue, WA 98006 (US). MITCHAM, Jennifer, Lynn; 16677 Northeast 88th		GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, K KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, M MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, S SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, Z' ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, U ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI pate (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, N SN, TD, TG). t, Published Without international search report and to be republish upon receipt of that report.	SB, CG, IK, SI, W, JG, TJ, FI, ent

(54) Title: COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

(57) Abstract

Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate tumor proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate tumor protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate tumor protein, or mRNA encoding such a protein, in a sample are also provided.

COMPOSITIONS AND METHODS FOR THERAPY AND DIAGNOSIS OF PROSTATE CANCER

TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate tumor protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate tumor protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments, the polypeptide comprises at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a tumor protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate tumor protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, vaccines are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and a non-specific immune response enhancer.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate tumor protein; and (b) a physiologically acceptable carrier.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a non-specific immune response enhancer.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a non-specific immune response enhancer.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate tumor protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic

kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate tumor polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate tumor polypeptide P502S. In each case, the number of γ -interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate tumor polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8⁺ cell line (3A-1) for a representative prostate tumor antigen (P501S). Figure 6A shows the results of a ⁵¹Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target rations as indicated.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12
SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16
SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1
SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9
SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4
SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17
SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17
SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12
SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12
SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862
SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862
SEQ ID NO: 14 is the determined 3' cDNA sequence for J1-13
SEQ ID NO: 15 is the determined 5' cDNA sequence for J1-13
SEQ ID NO: 16 is the determined 3' cDNA sequence for J1-19
SEQ ID NO: 17 is the determined 5' cDNA sequence for J1-19
SEQ ID NO: 18 is the determined 3' cDNA sequence for J1-25
SEQ ID NO: 19 is the determined 5' cDNA sequence for J1-25
SEQ ID NO: 20 is the determined 5' cDNA sequence for J1-24
SEQ ID NO: 21 is the determined 3' cDNA sequence for J1-24
SEQ ID NO: 22 is the determined 5' cDNA sequence for K1-58
SEQ ID NO: 23 is the determined 3' cDNA sequence for K1-58
SEQ ID NO: 24 is the determined 5' cDNA sequence for K1-63
SEQ ID NO: 25 is the determined 3' cDNA sequence for K1-63
SEQ ID NO: 26 is the determined 5' cDNA sequence for L1-4
SEQ ID NO: 27 is the determined 3' cDNA sequence for L1-4
SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14
SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14
SEQ ID NO: 30 is the determined 3' cDNA sequence for J1-12
SEQ ID NO: 31 is the determined 3' cDNA sequence for J1-16
SEQ ID NO: 32 is the determined 3' cDNA sequence for J1-21
SEQ ID NO: 33 is the determined 3' cDNA sequence for K1-48
SEQ ID NO: 34 is the determined 3' cDNA sequence for K1-55
SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2
SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6
SEQ ID NO: 37 is the determined 3' cDNA sequence for N1-1858
SEQ ID NO: 38 is the determined 3' cDNA sequence for N1-1860 $$
SEQ ID NO: 39 is the determined 3' cDNA sequence for N1-1861

SEO ID NO: 40 is the determined 3' cDNA sequence for N1-1864 SEO ID NO: 41 is the determined cDNA sequence for P5 SEO ID NO: 42 is the determined cDNA sequence for P8 SEO ID NO: 43 is the determined cDNA sequence for P9 SEO ID NO: 44 is the determined cDNA sequence for P18 SEQ ID NO: 45 is the determined cDNA sequence for P20 SEO ID NO: 46 is the determined cDNA sequence for P29 SEO ID NO: 47 is the determined cDNA sequence for P30 SEO ID NO: 48 is the determined cDNA sequence for P34 SEQ ID NO: 49 is the determined cDNA sequence for P36 SEO ID NO: 50 is the determined cDNA sequence for P38 SEO ID NO: 51 is the determined cDNA sequence for P39 SEO ID NO: 52 is the determined cDNA sequence for P42 SEQ ID NO: 53 is the determined cDNA sequence for P47 SEO ID NO: 54 is the determined cDNA sequence for P49 SEO ID NO: 55 is the determined cDNA sequence for P50 SEQ ID NO: 56 is the determined cDNA sequence for P53 SEQ ID NO: 57 is the determined cDNA sequence for P55 SEQ ID NO: 58 is the determined cDNA sequence for P60 SEQ ID NO: 59 is the determined cDNA sequence for P64 SEQ ID NO: 60 is the determined cDNA sequence for P65 SEQ ID NO: 61 is the determined cDNA sequence for P73 SEQ ID NO: 62 is the determined cDNA sequence for P75 SEQ ID NO: 63 is the determined cDNA sequence for P76 SEQ ID NO: 64 is the determined cDNA sequence for P79 SEQ ID NO: 65 is the determined cDNA sequence for P84 SEQ ID NO: 66 is the determined cDNA sequence for P68 SEQ ID NO: 67 is the determined cDNA sequence for P80 SEQ ID NO: 68 is the determined cDNA sequence for P82 SEQ ID NO: 69 is the determined cDNA sequence for U1-3064 SEQ ID NO: 70 is the determined cDNA sequence for U1-3065 SEQ ID NO: 71 is the determined cDNA sequence for V1-3692 SEQ ID NO: 72 is the determined cDNA sequence for 1A-3905 SEQ ID NO: 73 is the determined cDNA sequence for V1-3686 SEQ ID NO: 74 is the determined cDNA sequence for R1-2330

SEQ ID NO: 75 is the determined cDNA sequence for 1B-3976 SEQ ID NO: 76 is the determined cDNA sequence for V1-3679

SEO ID NO: 77 is the determined cDNA sequence for 1G-4736 SEO ID NO: 78 is the determined cDNA sequence for 1G-4738 SEQ ID NO: 79 is the determined cDNA sequence for 1G-4741 SEQ ID NO: 80 is the determined cDNA sequence for 1G-4744 SEO ID NO: 81 is the determined cDNA sequence for 1G-4734 SEO ID NO: 82 is the determined cDNA sequence for 1H-4774 SEQ ID NO: 83 is the determined cDNA sequence for 1H-4781 SEQ ID NO: 84 is the determined cDNA sequence for 1H-4785 SEQ ID NO: 85 is the determined cDNA sequence for 1H-4787 SEQ ID NO: 86 is the determined cDNA sequence for 1H-4796 SEQ ID NO: 87 is the determined cDNA sequence for 1I-4807 SEQ ID NO: 88 is the determined cDNA sequence for 1I-4810 SEQ ID NO: 89 is the determined cDNA sequence for 1I-4811 SEQ ID NO: 90 is the determined cDNA sequence for 1J-4876 SEQ ID NO: 91 is the determined cDNA sequence for 1K-4884 SEQ ID NO: 92 is the determined cDNA sequence for 1K-4896 SEQ ID NO: 93 is the determined cDNA sequence for 1G-4761 SEO ID NO: 94 is the determined cDNA sequence for 1G-4762 SEQ ID NO: 95 is the determined cDNA sequence for 1H-4766 SEO ID NO: 96 is the determined cDNA sequence for 1H-4770 SEQ ID NO: 97 is the determined cDNA sequence for 1H-4771 SEQ ID NO: 98 is the determined cDNA sequence for 1H-4772 SEO ID NO: 99 is the determined cDNA sequence for 1D-4297 SEQ ID NO: 100 is the determined cDNA sequence for 1D-4309 SEQ ID NO: 101 is the determined cDNA sequence for 1D.1-4278 SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288 SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283 SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304 SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296 SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280 SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S) SEO ID NO: 108 is the predicted amino acid sequence for F1-12 SEO ID NO: 109 is the determined full length cDNA sequence for J1-17 SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 SEO ID NO: 111 is the determined full length cDNA sequence for N1-1862

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 SEO ID NO: 115 is the determined cDNA sequence for P89 SEO ID NO: 116 is the determined cDNA sequence for P90 SEQ ID NO: 117 is the determined cDNA sequence for P92 SEQ ID NO: 118 is the determined cDNA sequence for P95 SEQ ID NO: 119 is the determined cDNA sequence for P98 SEQ ID NO: 120 is the determined cDNA sequence for P102 SEQ ID NO: 121 is the determined cDNA sequence for P110 SEQ ID NO: 122 is the determined cDNA sequence for P111 SEQ ID NO: 123 is the determined cDNA sequence for P114 SEQ ID NO: 124 is the determined cDNA sequence for P115 SEQ ID NO: 125 is the determined cDNA sequence for P116 SEQ ID NO: 126 is the determined cDNA sequence for P124 SEQ ID NO: 127 is the determined cDNA sequence for P126 SEQ ID NO: 128 is the determined cDNA sequence for P130 SEQ ID NO: 129 is the determined cDNA sequence for P133 SEQ ID NO: 130 is the determined cDNA sequence for P138 SEQ ID NO: 131 is the determined cDNA sequence for P143 SEQ ID NO: 132 is the determined cDNA sequence for P151 SEQ ID NO: 133 is the determined cDNA sequence for P156 SEQ ID NO: 134 is the determined cDNA sequence for P157 SEQ ID NO: 135 is the determined cDNA sequence for P166 SEQ ID NO: 136 is the determined cDNA sequence for P176 SEQ ID NO: 137 is the determined cDNA sequence for P178 SEQ ID NO: 138 is the determined cDNA sequence for P179 SEQ ID NO: 139 is the determined cDNA sequence for P185 SEQ ID NO: 140 is the determined cDNA sequence for P192 SEQ ID NO: 141 is the determined cDNA sequence for P201 SEQ ID NO: 142 is the determined cDNA sequence for P204 SEQ ID NO: 143 is the determined cDNA sequence for P208 SEQ ID NO: 144 is the determined cDNA sequence for P211 SEO ID NO: 145 is the determined cDNA sequence for P213 SEQ ID NO: 146 is the determined cDNA sequence for P219 SEQ ID NO: 147 is the determined cDNA sequence for P237 SEQ ID NO: 148 is the determined cDNA sequence for P239 SEQ ID NO: 149 is the determined cDNA sequence for P248

SEQ ID NO: 150 is the determined cDNA sequence for P251
SEQ ID NO: 151 is the determined cDNA sequence for P255
SEQ ID NO: 152 is the determined cDNA sequence for P256
SEQ ID NO: 153 is the determined cDNA sequence for P259
SEQ ID NO: 154 is the determined cDNA sequence for P260
SEQ ID NO: 155 is the determined cDNA sequence for P263
SEQ ID NO: 156 is the determined cDNA sequence for P264
SEQ ID NO: 157 is the determined cDNA sequence for P266
SEQ ID NO: 158 is the determined cDNA sequence for P270
SEQ ID NO: 159 is the determined cDNA sequence for P272
SEQ ID NO: 160 is the determined cDNA sequence for P278
SEQ ID NO: 161 is the determined cDNA sequence for P105
SEQ ID NO: 162 is the determined cDNA sequence for P107
SEQ ID NO: 163 is the determined cDNA sequence for P137
SEQ ID NO: 164 is the determined cDNA sequence for P194
SEQ ID NO: 165 is the determined cDNA sequence for P195
SEQ ID NO: 166 is the determined cDNA sequence for P196
SEQ ID NO: 167 is the determined cDNA sequence for P220
SEQ ID NO: 168 is the determined cDNA sequence for P234
SEQ ID NO: 169 is the determined cDNA sequence for P235
SEQ ID NO: 170 is the determined cDNA sequence for P243
SEQ ID NO: 171 is the determined cDNA sequence for P703P-DE1
SEQ ID NO: 172 is the predicted amino acid sequence for P703P-DE1
SEQ ID NO: 173 is the determined cDNA sequence for P703P-DE2
SEQ ID NO: 174 is the determined cDNA sequence for P703P-DE6
SEQ ID NO: 175 is the determined cDNA sequence for P703P-DE13
SEQ ID NO: 176 is the predicted amino acid sequence for P703P-DE13
SEQ ID NO: 177 is the determined cDNA sequence for P703P-DE14
SEQ ID NO: 178 is the predicted amino acid sequence for P703P-DE14
SEQ ID NO: 179 is the determined extended cDNA sequence for 1G-4736 $$
SEQ ID NO: 180 is the determined extended cDNA sequence for 1G-4738 $$
SEQ ID NO: 181 is the determined extended cDNA sequence for $1G-4741$
SEQ ID NO: 182 is the determined extended cDNA sequence for $1G-4744$
SEQ ID NO: 183 is the determined extended cDNA sequence for $1H-4774$
SEQ ID NO: 184 is the determined extended cDNA sequence for $1H-4781$
SEQ ID NO: 185 is the determined extended cDNA sequence for 1H-4785 $$
SEQ ID NO: 186 is the determined extended cDNA sequence for 1H-4787

SEQ ID NO: 187 is the determined extended cDNA sequence for 1H-4796 SEQ ID NO: 188 is the determined extended cDNA sequence for 1I-4807 SEQ ID NO: 189 is the determined 3' cDNA sequence for 1I-4810 SEQ ID NO: 190 is the determined 3' cDNA sequence for 1I-4811 SEQ ID NO: 191 is the determined extended cDNA sequence for 1J-4876 SEQ ID NO: 192 is the determined extended cDNA sequence for 1K-4884 SEQ ID NO: 193 is the determined extended cDNA sequence for 1K-4896 SEQ ID NO: 194 is the determined extended cDNA sequence for 1G-4761 SEQ ID NO: 195 is the determined extended cDNA sequence for 1G-4762 SEQ ID NO: 196 is the determined extended cDNA sequence for 1H-4766 SEQ ID NO: 197 is the determined 3' cDNA sequence for 1H-4770 SEQ ID NO: 198 is the determined 3' cDNA sequence for 1H-4771 SEQ ID NO: 199 is the determined extended cDNA sequence for 1H-4772 SEQ ID NO: 200 is the determined extended cDNA sequence for 1D-4309 SEQ ID NO: 201 is the determined extended cDNA sequence for 1D.1-4278 SEQ ID NO: 202 is the determined extended cDNA sequence for 1D-4288 SEQ ID NO: 203 is the determined extended cDNA sequence for 1D-4283 SEQ ID NO: 204 is the determined extended cDNA sequence for 1D-4304 SEQ ID NO: 205 is the determined extended cDNA sequence for 1D-4296 SEQ ID NO: 206 is the determined extended cDNA sequence for 1D-4280 SEQ ID NO: 207 is the determined cDNA sequence for 10-d8fwd SEQ ID NO: 208 is the determined cDNA sequence for 10-H10con SEO ID NO: 209 is the determined cDNA sequence for 11-C8rev SEQ ID NO: 210 is the determined cDNA sequence for 7.g6fwd SEQ ID NO: 211 is the determined cDNA sequence for 7.g6rev SEQ ID NO: 212 is the determined cDNA sequence for 8-b5fwd SEQ ID NO: 213 is the determined cDNA sequence for 8-b5rev SEQ ID NO: 214 is the determined cDNA sequence for 8-b6fwd SEQ ID NO: 215 is the determined cDNA sequence for 8-b6 rev SEQ ID NO: 216 is the determined cDNA sequence for 8-d4fwd SEQ ID NO: 217 is the determined cDNA sequence for 8-d9rev SEQ ID NO: 218 is the determined cDNA sequence for 8-g3fwd SEQ ID NO: 219 is the determined cDNA sequence for 8-g3rev SEQ ID NO: 220 is the determined cDNA sequence for 8-h11rev SEQ ID NO: 221 is the determined cDNA sequence for g-f12fwd SEQ ID NO: 222 is the determined cDNA sequence for g-f3rev SEQ ID NO: 223 is the determined cDNA sequence for P509S

SEO ID NO: 224 is the determined cDNA sequence for P510S SEQ ID NO: 225 is the determined cDNA sequence for P703DE5 SEQ ID NO: 226 is the determined cDNA sequence for 9-A11 SEQ ID NO: 227 is the determined cDNA sequence for 8-C6 SEQ ID NO: 228 is the determined cDNA sequence for 8-H7 SEQ ID NO: 229 is the determined cDNA sequence for JPTPN13 SEQ ID NO: 230 is the determined cDNA sequence for JPTPN14 SEO ID NO: 231 is the determined cDNA sequence for JPTPN23 SEO ID NO: 232 is the determined cDNA sequence for JPTPN24 SEO ID NO: 233 is the determined cDNA sequence for JPTPN25 SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30 SEO ID NO: 235 is the determined cDNA sequence for JPTPN34 SEQ ID NO: 236 is the determined cDNA sequence for PTPN35 SEO ID NO: 237 is the determined cDNA sequence for JPTPN36 SEO ID NO: 238 is the determined cDNA sequence for JPTPN38 SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39 SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40 SEO ID NO: 241 is the determined cDNA sequence for JPTPN41 SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42 SEO ID NO: 243 is the determined cDNA sequence for JPTPN45 SEO ID NO: 244 is the determined cDNA sequence for JPTPN46 SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51 SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56 SEQ ID NO: 247 is the determined cDNA sequence for PTPN64 SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65 SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67 SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76 SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84 SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85 SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86 SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87 SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88 SEQ ID NO: 256 is the determined cDNA sequence for JP1F1 SEQ ID NO: 257 is the determined cDNA sequence for JP1F2 SEQ ID NO: 258 is the determined cDNA sequence for JP1C2 SEQ ID NO: 259 is the determined cDNA sequence for JP1B1 SEQ ID NO: 260 is the determined cDNA sequence for JP1B2

SEQ ID NO: 261 is the determined cDNA sequence for JP1D3 SEO ID NO: 262 is the determined cDNA sequence for JP1A4 SEO ID NO: 263 is the determined cDNA sequence for JP1F5 SEO ID NO: 264 is the determined cDNA sequence for JP1E6 SEO ID NO: 265 is the determined cDNA sequence for JP1D6 SEQ ID NO: 266 is the determined cDNA sequence for JP1B5 SEQ ID NO: 267 is the determined cDNA sequence for JP1A6 SEQ ID NO: 268 is the determined cDNA sequence for JP1E8 SEQ ID NO: 269 is the determined cDNA sequence for JP1D7 SEQ ID NO: 270 is the determined cDNA sequence for JP1D9 SEQ ID NO: 271 is the determined cDNA sequence for JP1C10 SEO ID NO: 272 is the determined cDNA sequence for JP1A9 SEO ID NO: 273 is the determined cDNA sequence for JP1F12 SEQ ID NO: 274 is the determined cDNA sequence for JP1E12 SEO ID NO: 275 is the determined cDNA sequence for JP1D11 SEQ ID NO: 276 is the determined cDNA sequence for JP1C11 SEQ ID NO: 277 is the determined cDNA sequence for JP1C12 SEO ID NO: 278 is the determined cDNA sequence for JP1B12 SEQ ID NO: 279 is the determined cDNA sequence for JP1A12 SEQ ID NO: 280 is the determined cDNA sequence for JP8G2 SEO ID NO: 281 is the determined cDNA sequence for JP8H1 SEO ID NO: 282 is the determined cDNA sequence for JP8H2 SEO ID NO: 283 is the determined cDNA sequence for JP8A3 SEQ ID NO: 284 is the determined cDNA sequence for JP8A4 SEQ ID NO: 285 is the determined cDNA sequence for JP8C3 SEQ ID NO: 286 is the determined cDNA sequence for JP8G4 SEQ ID NO: 287 is the determined cDNA sequence for JP8B6 SEQ ID NO: 288 is the determined cDNA sequence for JP8D6 SEQ ID NO: 289 is the determined cDNA sequence for JP8F5 SEO ID NO: 290 is the determined cDNA sequence for JP8A8 SEQ ID NO: 291 is the determined cDNA sequence for JP8C7 SEO ID NO: 292 is the determined cDNA sequence for JP8D7 SEO ID NO: 293 is the determined cDNA sequence for P8D8 SEO ID NO: 294 is the determined cDNA sequence for JP8E7 SEO ID NO: 295 is the determined cDNA sequence for JP8F8 SEQ ID NO: 296 is the determined cDNA sequence for JP8G8 SEQ ID NO: 297 is the determined cDNA sequence for JP8B10 SEQ ID NO: 298 is the determined cDNA sequence for JP8C10 SEO ID NO: 299 is the determined cDNA sequence for JP8E9 SEQ ID NO: 300 is the determined cDNA sequence for JP8E10 SEQ ID NO: 301 is the determined cDNA sequence for JP8F9 SEQ ID NO: 302 is the determined cDNA sequence for JP8H9 SEQ ID NO: 303 is the determined cDNA sequence for JP8C12 SEQ ID NO: 304 is the determined cDNA sequence for JP8E11 SEO ID NO: 305 is the determined cDNA sequence for JP8E12 SEO ID NO: 306 is the amino acid sequence for the peptide PS2#12 SEO ID NO: 307 is the determined cDNA sequence for P711P SEQ ID NO: 308 is the determined cDNA sequence for P712P SEO ID NO: 309 is the determined cDNA sequence for CLONE23 SEQ ID NO: 310 is the determined cDNA sequence for P774P SEQ ID NO: 311 is the determined cDNA sequence for P775P SEO ID NO: 312 is the determined cDNA sequence for P715P SEQ ID NO: 313 is the determined cDNA sequence for P710P SEQ ID NO: 314 is the determined cDNA sequence for P767P SEO ID NO: 315 is the determined cDNA sequence for P768P SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5 SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5 SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26 SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26 SEO ID NO: 330 is the determined cDNA sequence for P703PX-23 SEO ID NO: 331 is the predicted amino acid sequence for P703PX-23 SEO ID NO: 332 is the determined full length cDNA sequence for P509S SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as SEQ ID NO: 334 is the determined cDNA sequence for P714P SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3) SEQ ID NO: 336 is the predicted amino acid sequence for P705P SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10 SEQ ID NO: 338 is the amino acid sequence of the peptide p5 SEQ ID NO: 339 is the predicted amino acid sequence of P509S SEQ ID NO: 340 is the determined cDNA sequence for P778P SEQ ID NO: 341 is the determined cDNA sequence for P786P

SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo sapiens MM46 mRNA

SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo sapiens mRNA for E-cadherin

SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S

SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID

NO: 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID

NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO:386 is the cDNA sequence for 23320.

SEQ ID NO:387 is the cDNA sequence for CGI-69.

SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO:389 is the cDNA sequence for 23379.

SEQ ID NO:390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571. SEQ ID NO:415 is the cDNA sequence for 22572. SEQ ID NO:416 is the cDNA sequence for 22573. SEQ ID NO:417 is the cDNA sequence for 22573. SEQ ID NO:418 is the cDNA sequence for 22575. SEQ ID NO:419 is the cDNA sequence for 22580. SEQ ID NO:420 is the cDNA sequence for 22581. SEQ ID NO:421 is the cDNA sequence for 22582. SEQ ID NO:422 is the cDNA sequence for 22583. SEQ ID NO:423 is the cDNA sequence for 22584. SEQ ID NO:424 is the cDNA sequence for 22585. SEQ ID NO:425 is the cDNA sequence for 22586. SEQ ID NO:426 is the cDNA sequence for 22587. SEQ ID NO:427 is the cDNA sequence for 22588. SEQ ID NO:428 is the cDNA sequence for 22589. SEQ ID NO:429 is the cDNA sequence for 22590. SEQ ID NO:430 is the cDNA sequence for 22591. SEO ID NO:431 is the cDNA sequence for 22592. SEO ID NO:432 is the cDNA sequence for 22593. SEQ ID NO:433 is the cDNA sequence for 22594. SEQ ID NO:434 is the cDNA sequence for 22595. SEQ ID NO:435 is the cDNA sequence for 22596. SEQ ID NO:436 is the cDNA sequence for 22847. SEQ ID NO:437 is the cDNA sequence for 22848. SEQ ID NO:438 is the cDNA sequence for 22849. SEQ ID NO:439 is the cDNA sequence for 22851. SEQ ID NO:440 is the cDNA sequence for 22852. SEQ ID NO:441 is the cDNA sequence for 22853. SEQ ID NO:442 is the cDNA sequence for 22854. SEQ ID NO:443 is the cDNA sequence for 22855. SEQ ID NO:444 is the cDNA sequence for 22856. SEQ ID NO:445 is the cDNA sequence for 22857. SEQ ID NO:446 is the cDNA sequence for 23601. SEQ ID NO:447 is the cDNA sequence for 23602. SEQ ID NO:448 is the cDNA sequence for 23605. SEQ ID NO:449 is the cDNA sequence for 23606. SEQ ID NO:450 is the cDNA sequence for 23612.

SEQ ID NO:451 is the cDNA sequence for 23614.

SEQ ID NO:452 is the cDNA sequence for 23618.

SEQ ID NO:453 is the cDNA sequence for 23622.

SEQ ID NO:454 is the cDNA sequence for folate hydrolase.

SEQ ID NO:455 is the cDNA sequence for LIM protein.

SEQ ID NO:456 is the cDNA sequence for a known gene.

SEQ ID NO:457 is the cDNA sequence for a known gene.

SEQ ID NO:458 is the cDNA sequence for a previously identified gene.

SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NOs:462-467 are cDNA sequences for known genes.

SEQ ID NOs:468-471 are cDNA sequences for P710P.

SEQ ID NO:472 is a cDNA sequence for P1001C.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. compositions described herein may include prostate tumor polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate tumor protein or a variant thereof. A "prostate tumor protein" is a protein that is expressed in prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a normal tissue, as determined using a representative assay provided herein. Certain prostate tumor proteins are tumor proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate tumor proteins. Sequences of polynucleotides encoding certain tumor proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Sequences of polypeptides comprising at least a portion of a tumor protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380 and 383.

PROSTATE TUMOR PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate tumor protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate tumor protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate tumor protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a prostate tumor protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native tumor protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate tumor protein or a portion thereof.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50,

in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 Methods in Enzymology vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) CABIOS 5:151-153; Myers, E.W. and Muller W. (1988) CABIOS 4:11-17; Robinson, E.D. (1971) Comb. Theor 11:105; Santou, N. Nes, M. (1987) Mol. Biol. Evol. 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Proc. Natl. Acad., Sci. USA 80:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate tumor protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to

the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate tumor cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (e.g., a prostate tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by nick-translation or end-labeling with ³²P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using

standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

One such amplification technique is inverse PCR (see Triglia et al., Nucl. Acids Res. 16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., PCR Methods Applic. 1:111-19, 1991) and walking PCR (Parker et al., Nucl. Acids. Res. 19:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence.

Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate tumor protein are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472. Isolation of these

polynucleotides is described below. Each of these prostate tumor proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis. Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., DNA 2:183, 1983). Alternatively, RNA molecules may be generated by in vitro or in vivo transcription of DNA sequences encoding a prostate tumor protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated in vivo (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate tumor polypeptide, and administering the transfected cells to the patient).

A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a tumor protein. Antisense technology can be used to control gene expression through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., In Huber and Carr, Molecular and Immunologic Approaches, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such

as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques. For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary skill in the art.

Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle *in vitro* and *in vivo* is a liposome (*i.e.*, an artificial membrane vesicle). The preparation and use of such systems is well known in the art.

PROSTATE TUMOR POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate tumor protein or a variant thereof, as described herein. As noted above, a "prostate tumor protein" is a protein that is expressed by prostate tumor cells. Proteins that are prostate tumor proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from

the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

An "immunogenic portion," as used herein is a portion of a protein that is recognized (*i.e.*, specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate tumor protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, Fundamental Immunology, 3rd ed., 243-247 (Raven Press, 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known techniques. An immunogenic portion of a native prostate tumor protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those of ordinary skill in the art, such as those described in Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate tumor protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate tumor protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein.

Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques. Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are

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E. coli, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, J. Am. Chem. Soc. 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into

the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene 40*:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA 83*:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (e.g., the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in E. coli (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as

amidase LYTA (encoded by the LytA gene; Gene 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of E. coli C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see Biotechnology 10:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate tumor protein. As used herein, an antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate tumor protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate tumor protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10³ L/mol. The binding constant may be determined using methods well known in the art.

Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate tumor protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from

patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (e.g., mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient

time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ⁹⁰Y, ¹²³I, ¹²⁵I, ¹³¹I, ¹⁸⁶Re, ¹⁸⁸Re, ²¹¹At, and ²¹²Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and

thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (e.g., U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (e.g., U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (e.g., U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (e.g., U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T CELLS

Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate tumor protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the CEPRATE™ system, available from CellPro Inc., Bothell WA (*see also* U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate tumor polypeptide, polynucleotide encoding a prostate tumor polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate tumor polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate tumor polypeptide if the T cells kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., Cancer Res. 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate tumor polypeptide (100 ng/ml - 100 μg/ml, preferably 200 ng/ml - 25 μg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience

(Greene 1998)). T cells that have been activated in response to a prostate tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Prostate tumor protein-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a prostate tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate tumor protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and a non-specific immune response enhancer. A non-specific immune response enhancer may be any substance that enhances an immune response to an exogenous antigen. Examples of non-specific immune response enhancers include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998,

and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as Bacillus-Calmette-Guerrin) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (e.g., vaccinia or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., Proc. Natl. Acad. Sci. USA 86:317-321, 1989; Flexner et al., Ann. N.Y. Acad. Sci. 569:86-103, 1989; Flexner et al., Vaccine 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, Biotechniques 6:616-627, 1988; Rosenfeld et al., Science 252:431-434, 1991; Kolls et al., Proc. Natl. Acad. Sci. USA 91:215-219, 1994; Kass-Eisler et al., Proc. Natl. Acad. Sci. USA 90:11498-11502, 1993; Guzman et al., Circulation 88:2838-2848, 1993; and Guzman et al., Cir. Res. 73:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be "naked," as described, for example, in Ulmer et al., Science 259:1745-1749, 1993 and reviewed by Cohen, Science 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

Such compositions may also comprise buffers (e.g., neutral buffered saline or phosphate buffered saline), carbohydrates (e.g., glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA or glutathione, adjuvants (e.g., aluminum hydroxide) and/or

preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of non-specific immune response enhancers may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bortadella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN-γ, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6, IL-10 and TNF-β) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; see US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example, an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is

quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release formulation (*i.e.*, a formulation such as a capsule or sponge that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med. 50*:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*) and based on the lack of differentiation markers of B cells (CD19 and CD20), T cells (CD3), monocytes (CD14) and natural killer cells (CD56), as determined using standard assays. Dendritic cells may, of course, be engineered to express specific cell-

surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see Zitvogel et al.*, *Nature Med. 4*:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcy receptor, mannose receptor and DEC-205 marker. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (e.g., CD54 and CD11) and costimulatory molecules (e.g., CD40, CD80 and CD86).

APCs may generally be transfected with a polynucleotide encoding a prostate tumor protein (or portion or other variant thereof) such that the prostate tumor polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place ex vivo, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs in vivo. In vivo and ex vivo transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., Immunology and cell Biology 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the prostate tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that

provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor. Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as CD8+ cytotoxic T lymphocytes and CD4+ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein

may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al., Immunological Reviews 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (e.g., by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to nonvaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 100 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such

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a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or more prostate tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G, protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding

agent. Suitable polypeptides for use within such assays include full length prostate tumor proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20TM. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred

embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., Clinical Epidemiology: A Basic Science for Clinical Medicine, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1µg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate tumor protein in a biological sample. Within certain methods, a biological sample comprising CD4+ and/or CD8+ T cells isolated from a patient is incubated with a prostate tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated in vitro for 2-9 days (typically 4 days) at 37°C with prostate tumor polypeptide (e.g., $5 - 25 \mu g/ml$). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a prostate tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate tumor protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate tumor protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers

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comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375 and 381. Techniques for both PCR based assays and hybridization assays are well known in the art (see, for example, Mullis et al., Cold Spring Harbor Symp. Quant. Biol., 51:263, 1987; Erlich ed., PCR Technology, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate tumor protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate tumor protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate tumor protein.

The following Examples are offered by way of illustration and not by way of limitation.

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EXAMPLES

EXAMPLE 1

ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate tumor poly A* RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A* RNA was then purified using a Qiagen oligotex spin column mRNA purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the Notl/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with Notl. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/Notl site of pCDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64 x 10⁷ independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3 x 10⁶ independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara et al. (Blood, 84:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as follows. Normal pancreas cDNA library (70 µg) was digested with EcoRI, Notl, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 µl of

 H_2O , heat-denatured and mixed with 100 µl (100 µg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 µl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 µl H_2O to form the driver DNA.

To form the tracer DNA, 10 μg prostate tumor cDNA library was digested with BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 μl H₂O. Tracer DNA was mixed with 15 μl driver DNA and 20 μl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 μl H₂O, mixed with 8 μl driver DNA and 20 μl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively, with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human

autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 µg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to R. norvegicus mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted

amino acid sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein, mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and

prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4283, 1D-4283, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339.

EXAMPLE 2 DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for the representative prostate tumor polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 1-2 μg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 0 C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed using β -actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β -actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that

F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancrease, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney, but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression

in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis et al. (Proc. Natl. Acad. Sci. USA 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES
BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated

and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of 2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However, substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the microarray technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung, colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX 23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold overexpression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal prostate tissues (n=4), but background to low expression levels in all normal tissues.

Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

EXAMPLE 4 SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following

lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat norvegicus cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to G. gallus dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO: 341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID NO: 350-365.

EXAMPLE 6 PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTIL LINES

6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2.1 (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID NO: 8), as described by Theobald et al., Proc. Natl. Acad. Sci. USA 92:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-Ab binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6 x 106 cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10⁻⁵ M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells (5 x 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, Science 258:815-818, 1992) and 3 x 106/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were

restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2.1 expressing) transduced with P502S than against control fibroblasts. An example is presented in Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2.1 molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, et al, J. Immunol., 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2.1 were immunized as described by Theobald et al. (*Proc. Natl. Acad. Sci. USA 92*:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5μg of P1S #10 and 120μg of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6 x 10⁶ cells/ml in complete media (as described above) and cultured in the presence of irradiated (3000 rads) P1S#10-pulsed (2μ g/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7μg/ml dextran sulfate and 25μg/ml LPS for 3 days). Six days later cells (5 x 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3 x 10⁶/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were restimulated on a weekly

basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10⁴ cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10⁵ cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7 ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE TUMOR POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed in vitro to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (Critical Reviews in Immunology 18:65-75, 1998). The resulting CD8⁺ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a y-interferon ELISPOT assay (see Lalvani et al., J. Exp. Med. 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10⁴ fibroblasts in the presence of 3 μg/ml human β₂-microglobulin and 1 μg/ml P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control, fibroblasts transduced with HER-2/neu. Prior to the assay, the fibroblasts were treated with 10 ng/ml y-interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ-interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of y-interferon spots with increasing numbers of T cells on fibroblasts pulsed with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ-interferon spots with increasing numbers of T

cells on fibroblasts transduced to express the P502S gene but not the HER-2/neu gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

EXAMPLE 8 PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION WITH A PROSTATE ANTIGEN

The prostate tumor antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 µg VR10132-P501S either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed A2-restricted CTL epitope.

EXAMPLE 9

GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND STIMULATION TECHNIQUES WITH PROSTATE TUMOR ANTIGEN

Using *in vitro* whole-gene priming with P501S-retrovirally transduced autologous fibroblasts (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon-γ ELISPOT analysis as described above. Using a panel of HLA-mismatched fibroblast lines transduced with P501S, these CTL lines were shown to be restricted HLA-A2 class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and

priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S. Following four stimulation cycles, CD8+ T cell lines were identified that specifically produced interferon-γ when stimulated with P501S-transduced autologous fibroblasts. The P501S-specific activity could be sustained by the continued stimulation of the cultures with P501S-transduced fibroblasts in the presence of IL-15. A panel of HLA-mismatched fibroblast lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon-γ in an ELISPOT assay, the P501S specific response was shown to be restricted by HLA-A2. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

EXAMPLE 10 IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A PROSTATE TUMOR ANTIGEN

The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2 transgenic mice with p5 leads to the generation of CTL lines which recognize a variety of P703P transduced target cells expressing either HLA-A2Kb or HLA-A2. Specifically, HLA-A2 transgenic mice were immunized subcutaneously in the footpad with 100 µg of p5 peptide together with 140 µg of hepatitis B virus core peptide (a Th peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were identified.

Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with p5 peptide and cultured with GM-CSF and IL-4 together with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis

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Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with p5 peptide and cultured with GM-CSF and IL-4 together with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis

with p5-pulsed monocytes. Five to six weeks after initiation of the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated.

EXAMPLE 11 EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly expressed in breast tumor, prostate tumor, normal prostate tumor and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

EXAMPLE 12 ELICITATION OF PROSTATE TUMOR ANTIGEN-SPECIFIC CTL RESPONSES IN HUMAN BLOOD

This Example illustrates the ability of a prostate tumor antigen to elicit a CTL response in blood of normal humans.

Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8+ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL transduced to

express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxity assays (⁵¹Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see* above and Lalvani et al., *J. Exp. Med. 186*:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

EXAMPLE 13 IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of certain prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

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Table I
Summary of Prostate Tumor Antigens

Known Genes	Previously identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	8
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang(23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	

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transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate

tissues as compared to other normal tissues tested. It was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It was overexpressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97% of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

EXAMPLE 14 IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY ELECTRONIC SUBTRACTION

This Example describes the use of an electronic subtraction technique to identify prostate tumor antigens.

Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA 95*:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups, Plus (normal prostate and prostate tumor libraries, and breast cell lines, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

<u>Table II</u> Prostate cDNA Libraries and ESTs

Library	# of Libraries	# of ESTs	
Plus	25	43,482	
Normal	11	18,875	
Tumor	11	21,769	
Cell lines	3	2,838	
Minus	166		
Other	287		

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones found in the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones found in the Plus, Minus and Other group libraries, but the expression in the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones found in Plus, Minus and Other group libraries, but the expression in the Plus group is higher than the expression in the Minus group. This analysis identified 4,345 breast clusters (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

<u>Table III</u>

Prostate Cluster Summary

	# of # of EST	
Туре	Superclusters Ordere	
1	688	677
2	2899	2484
3	. 85	11
4	673	0
Total	4345	3172

The inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor cDNA was at least three times the level in normal prostate cDNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NOs:401-453, with certain novel sequences shown in SEQ ID NOs:407, 413, 416-419, 422, 426, 427 and 450.

<u>Table IV</u> Prostate-tumor Specific Clones

SEQ ID NO.	Sequence	Comments
	Designation	
401	22545	previously identified P1000C
402	22547	previously identified P704P

403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57

439	22851	PAP
440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

EXAMPLE 15 FURTHER IDENTIFICATION OF PROSTATE TUMOR ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate tumor polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NOs:454-467. Of these sequences SEQ ID NOs:459-461 correspond to novel genes. The others (SEQ ID NOs:454-458 and 461-467) correspond to known sequences.

EXAMPLE 16 FURTHER CHARACTERIZATION OF PROSTATE TUMOR ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic ABI Sequencer. Four sequences were obtained, and are presented in SEQ ID NOs:468-471.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

CLAIMS

- 1. An isolated polypeptide comprising at least an immunogenic portion of a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (a) sequences recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472;
- (b) sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and
 - (c) complements of any of the sequence of (a) or (b).
- 2. An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotide sequences.
- 3. An isolated polypeptide comprising a sequence recited in any one of SEO ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339 and 383.
- 4. An isolated polynucleotide encoding at least 15 amino acid residues of a prostate tumor protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigenspecific antisera is not substantially diminished, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434,

435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.

- 5. An isolated polynucleotide encoding a prostate tumor protein, or a variant thereof, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing sequences.
- 6. An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
- 7. An isolated polynucleotide comprising a sequence that hybridizes, under moderately stringent conditions, to a sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
- 8. An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.
- 9. An expression vector comprising a polynucleotide according to any one of claims 4-7.
- 10. A host cell transformed or transfected with an expression vector according to claim 9.
 - 11. An expression vector comprising a polynucleotide according claim 8.

- 12. A host cell transformed or transfected with an expression vector according to claim 11.
- 13. A pharmaceutical composition comprising a polypeptide according to claim 1, in combination with a physiologically acceptable carrier.
- 14. A vaccine comprising a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 15. A vaccine according to claim 14, wherein the non-specific immune response enhancer is an adjuvant.
- 16. A vaccine according to claim 14, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 17. A pharmaceutical composition comprising a polynucleotide according to claim 4, in combination with a physiologically acceptable carrier.
- 18. A vaccine comprising a polynucleotide according to claim 4, in combination with a non-specific immune response enhancer.
- 19. A vaccine according to claim 18, wherein the non-specific immune response enhancer is an adjuvant.
- 20. A vaccine according to claim 18, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 21. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate tumor protein that comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472 or a complement of any of the foregoing polynucleotide sequences.

- 22. A pharmaceutical composition comprising an antibody or fragment thereof according to claim 18, in combination with a physiologically acceptable carrier.
- 23. A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.
- 24. A pharmaceutical composition according to claim 23, wherein the antigen presenting cell is a dendritic cell or a macrophage.
- 25. A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a non-specific immune response enhancer.
- 26. A vaccine according to claim 25, wherein the non-specific immune response enhancer is an adjuvant.
- 27. A vaccine according to claim 25, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 28. A vaccine according to claim 25, wherein the antigen-presenting cell is a dendritic cell.
- 29. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.
- 30. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a polynucleotide according to claim 4, and thereby inhibiting the development of a cancer in the patient.
- 31. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antibody or antigen-binding fragment thereof according to claim 21, and thereby inhibiting the development of a cancer in the patient.

- 32. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide according to claim 1, and thereby inhibiting the development of a cancer in the patient.
- 33. A method according to claim 32, wherein the antigen-presenting cell is a dendritic cell.
- 34. A method according to any one of claims 29-32, wherein the cancer is prostate cancer.
- 35. A fusion protein comprising at least one polypeptide according to claim 1.
- 36. A fusion protein according to claim 35, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.
- 37. A fusion protein according to claim 35, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.
- 38. A fusion protein according to claim 35, wherein the fusion protein comprises an affinity tag.
- 39. An isolated polynucleotide encoding a fusion protein according to claim 35.
- 40. A pharmaceutical composition comprising a fusion protein according to claim 32, in combination with a physiologically acceptable carrier.
- 41. A vaccine comprising a fusion protein according to claim 35, in combination with a non-specific immune response enhancer.
- 42. A vaccine according to claim 41, wherein the non-specific immune response enhancer is an adjuvant.

- 43. A vaccine according to claim 41, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 44. A pharmaceutical composition comprising a polynucleotide according to claim 40, in combination with a physiologically acceptable carrier.
- 45. A vaccine comprising a polynucleotide according to claim 40, in combination with a non-specific immune response enhancer.
- 46. A vaccine according to claim 45, wherein the non-specific immune response enhancer is an adjuvant.
- 47. A vaccine according to claim 45, wherein the non-specific immune response enhancer induces a predominantly Type I response.
- 48. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 40 or claim 44.
- 49. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 41 or claim 45.
- 50. A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
 - (ii) complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate tumor protein from the sample.

51. A method according to claim 50, wherein the biological sample is blood or a fraction thereof.

- 52. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.
- 53. A method for stimulating and/or expanding T cells specific for a prostate tumor protein, comprising contacting T cells with one or more of:
 - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); and/or
- (iv) an antigen presenting cell that expresses a polypeptide of (i) or (ii); under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.
- 54. An isolated T cell population, comprising T cells prepared according to the method of claim 53.
- 55. A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 54.
- 56. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
 - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

- 57. A method for inhibiting the development of a cancer in a patient, comprising the steps of:
- (a) incubating CD4⁺ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:
 - (i) a polypeptide according to claim 1;
- (ii) a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NOs: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472;
 - (iii) a polynucleotide encoding a polypeptide of (i) or (ii); or
- (iv) an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

- (b) cloning at least one proliferated cell; and
- (c) administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.
- 58. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:
- (i) polynucleotides recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472; and
 - (ii) complements of the foregoing polynucleotides:
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (c) comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 59. A method according to claim 58, wherein the binding agent is an antibody.
- 60. A method according to claim 59, wherein the antibody is a monoclonal antibody.

- 61. A method according to claim 58, wherein the cancer is prostate cancer.
- 62. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of polypeptide that binds to the binding agent;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 63. A method according to claim 62, wherein the binding agent is an antibody.
- 64. A method according to claim 63, wherein the antibody is a monoclonal antibody.
- 65. A method according to claim 62, wherein the cancer is a prostate cancer.
- 66. A method for determining the presence or absence of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

- (c) comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.
- 67. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 68. A method according to claim 66, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
- 69. A method for monitoring the progression of a cancer in a patient, comprising the steps of:
- (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 or 384-472, or a complement of any of the foregoing polynucleotides;
- (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;
- (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and
- (d) comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.
- 70. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.
- 71. A method according to claim 69, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.
 - 72. A diagnostic kit, comprising:
 - (a) one or more antibodies according to claim 21; and
 - (b) a detection reagent comprising a reporter group.

- 73. A kit according to claim 72, wherein the antibodies are immobilized on a solid support.
- 74. A kit according to claim 73, wherein the solid support comprises nitrocellulose, latex or a plastic material.
- 75. A kit according to claim 72, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.
- 76. A kit according to claim 72, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups, enzymes, biotin and dye particles.
- 77. An oligonucleotide comprising 10 to 40 nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate tumor protein, wherein the tumor protein comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472, or a complement of any of the foregoing polynucleotides.
- 78. A oligonucleotide according to claim 77, wherein the oligonucleotide comprises 10-40 nucleotides recited in any one of SEQ ID NOs:2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471 or 472.
 - 79. A diagnostic kit, comprising:
 - (a) an oligonucleotide according to claim 77; and
- (b) a diagnostic reagent for use in a polymerase chain reaction or hybridization assay.

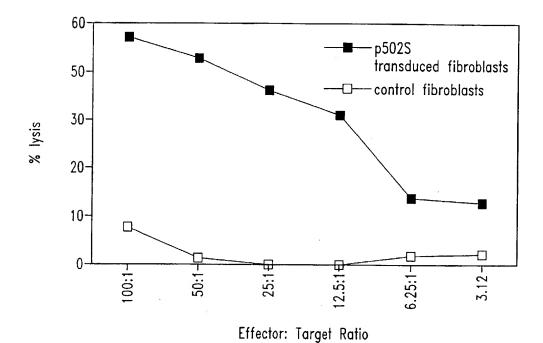


Fig. 1

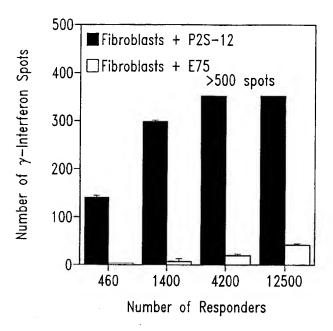


Fig. 2A

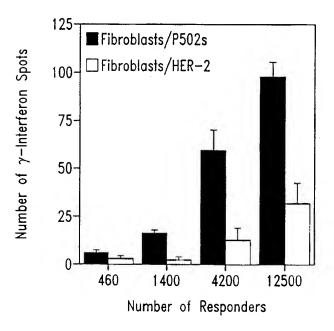
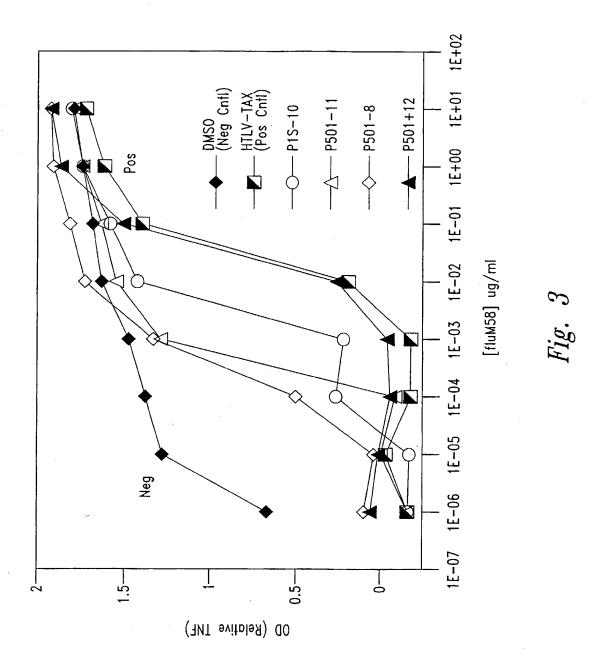


Fig. 2B

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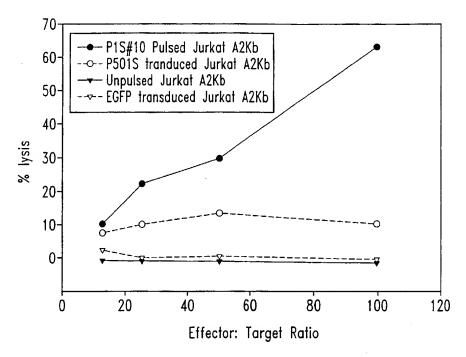


Fig. 4

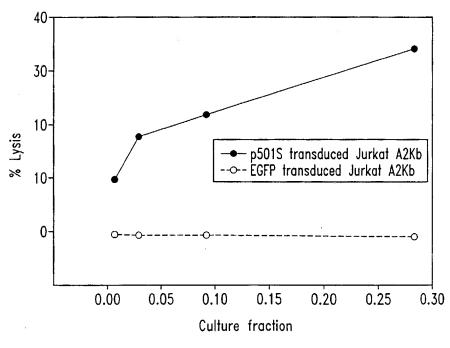
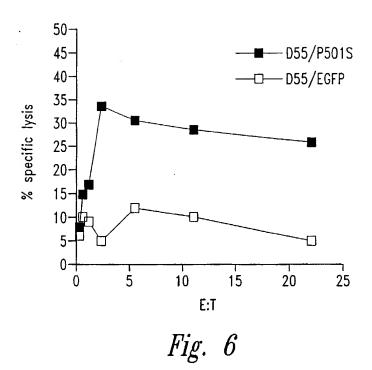
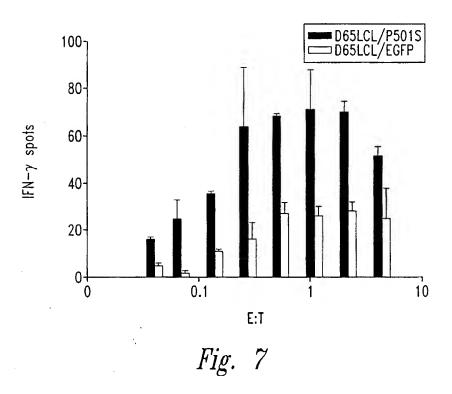


Fig. 5





SUBSTITUTE SHEET (RULE 26)

SEQUENCE LISTING

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caggecetaa geetggaget eeetteeeta atggacaegt gggtgetgga ggeagtggee
                                                                       300
tgctcccacc tccacccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg
                                                                       360
tggtgggtga gcccaccgan gccagggtgg ttccgggccg gggcatctgc ctggacctcg
                                                                       420
ccatcctgga tagtgcttcc tgctgtccca ngtggcccca tccctgttta tgggctccat
                                                                       480
tgtccagetc agccagtctg tcactgccta tatggtgtct gccgcaggcc tgggtctggt
                                                                       540
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcq
                                                                       600
ttaaaaaatt ccagcaacat tgggggtgga aggcctgcct cactgggtcc aactccccgc
                                                                       660
tectgttaac cecatgggge tgeeggettg geegecaatt tetgttgetg ceaaantnat
                                                                       720
gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtng
                                                                       780
ggngttccc
                                                                       789
```

<213> Homo sapien

```
<210> 11
      <211> 772
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(772)
      <223> n = A, T, C \text{ or } G
      <400> 11
cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac
                                                                        60
tttgttaaat aaataagtta aatatttaaa tgcctgtgtc tctgtgatgg caacagaagg
                                                                       120
accaacaggc cacatcctga taaaaggtaa gagggggtg gatcagcaaa aagacagtgc
                                                                       180
tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata
                                                                       240
actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag
                                                                       300
ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt
                                                                       360
tattcagete ccaaaaacee ttetetaggt gtgtetcaac taggaggeta getgttaace
                                                                       420
ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc
                                                                       480
ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana
                                                                       540
aactggggaa aaaagaaaag gacgcccan ccccagctg tgcanctacg cacctcaaca
                                                                       600
gcacagggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact ngqqqqqqa
                                                                       660
acceeggeac ecenangggg gttaacagga anengggnaa entggaacec aattnaggea
                                                                       720
ggcccnccac cccnaatntt gctgggaaat ttttcctccc ctaaattntt tc
                                                                       772
      <210> 12
      <211> 751
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(751)
      \langle 223 \rangle n = A,T,C or G
      <400> 12
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
                                                                        60
agetgattga ageaaceete taetttttgg tegtgageet tttgettggt geaggtttea
                                                                       120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                       180
aagtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc
                                                                       240
atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttqatqqca
                                                                       300
ggcactacca gcaacgtcág ggaagtgctc agccattgtg gtgtacacca aggcqaccac
                                                                       360
agcagetgen aceteageaa tgaagatgan gaggangatq aaqaagaacq tenegaqqqe
                                                                       420
acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna
                                                                       480
cnccggctgc gatgaagaaa tnaccccncg ttgacaaact tgcatggcac tggganccac
                                                                       540
agtggcccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactq
                                                                       600
ccaacagggg ctgccccacn cncnnaacga tganccnatt gnacaagatc tncntggtct
                                                                       660
tnatnaacht gaaccetgen tngtggetee tgtteaggne ennggeetga ettetnaann
                                                                       720
aangaacten gaagneecca enggananne g
                                                                       751
      <210> 13
      <211> 729
      <212> DNA
```

```
<220>
      <221> misc feature
      <222> (1)...(729)
      <223> n = A,T,C \text{ or } G
gagecaggeg teectetgee tgeccaetea gtggcaacae eegggagetg ttttqteett
                                                                        60
tqtggancct cagcagtncc ctctttcaga actcantgcc aaganccctg aacaggagcc
                                                                       120
accatgoagt getteagett cattaagace atgatgatee tetteaattt geteatettt
                                                                       180
ctqtqtqqtq caqccctqtt ggcaqtgggc atctgggtgt caatcgatgg ggcatccttt
                                                                       240
                                                                       300
ctqaaqatct tcgqgccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc
                                                                       360
ctcatcgcag coggogttgt ggtcttagct ctaggtttcc tgggctgcta tggtgctaag
actgagagea agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct
                                                                       420
qaqqttqcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt
                                                                       480
tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaanact tcactcaagt
                                                                       540
gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt
                                                                       600
gaagantcac ctacttcaaa gaaaanagtg cctttccccc atttctgttg caattgacaa
                                                                       660
acqtcccaa cacagccaat tgaaaacctg cacccaaccc aaangggtcc ccaaccanaa
                                                                       720
                                                                       729
attnaaggg
      <210> 14
      <211> 816
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(816)
      <223> n = A,T,C or G
      <400> 14
tgctcttcct caaaqttqtt cttqttgcca taacaaccac cataggtaaa gcgggcgcag
                                                                        60
tqttcqctqa agggqttgta gtaccagcgc gggatgctct ccttgcagag tcctgtgtct
                                                                       120
qqcaqqtcca cgcaqtgccc tttgtcactg gggaaatgga tgcgctggag ctcgtcaaag
                                                                       180
ccactcgtgt atttttcaca ggcagcctcg tccgacgcgt cggggcagtt gggggtgtct
                                                                       240
                                                                       300
tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaactg ggtgggctga
cangtqccaq aqcacactqq atggcgcctt tccatgnnan gggccctgng ggaaagtccc
                                                                       360
tganccccan anctgcctct caaangcccc accttgcaca ccccgacagg ctagaatgga
                                                                       420
atcttcttcc cqaaaqqtaq ttnttcttgt tgcccaancc anccccntaa acaaactctt
                                                                       480
qcanatctqc tccqnqqqq tcntantacc ancqtqqqaa aagaacccca ggcngcqaac
                                                                       540
caancttgtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna
                                                                       600
ctqtnnanct ttagnccntg gtcctcntgg gttgnncttg aacctaatcn ccnntcaact
                                                                       660
gggacaaggt aantngcent cetttnaatt eeenanentn eeecetggtt tggggttttn
                                                                       720
cnenctecta ecceagaaan neegtgttee ecceeaacta ggggeenaaa cennttntte
                                                                       780
                                                                       816
cacaaccetn ccccacccac gggttcngnt ggttng
      <210> 15
      <211> 783
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(783)
      \langle 223 \rangle n = A,T,C or G
```

```
<400> 15
ccaaggectg ggcaggcata nacttgaagg tacaacccca ggaacccctg gtgctgaagg
                                                                        60
atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagaga
                                                                       120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga
                                                                       180
cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca
                                                                       240
ccaagcagac agaagactac tgcctcgcat ccaacaangt gggtcgctgc cggggctctt
                                                                       300
teccaegetg gtactatgae eccaeggage agatetgeaa gagtttegtt tatggagget
                                                                       360
gettgggcaa caagaacaac tacetteggg aagaagagtg cattetance tgtengggtg
                                                                       420
tgcaaggtgg gcctttgana ngcanctctg gggctcangc gactttcccc cagggcccct
                                                                       480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gcccacccag ttccgctgca
                                                                       540
ncaatggctg ctgcatcnac antitcctng aattgtgaca acacccccca ntgcccccaa
                                                                       600
ccctcccaac aaagcttccc tgttnaaaaa tacnccantt ggcttttnac aaacncccqq
                                                                       660
cnecteentt tteecenntn aacaaagge netngenttt gaactgeeen aaccenggaa
                                                                       720
tetneenngg aaaaantnee ceeeetggtt eetnnaanee eeteenemaa anetneeeee
                                                                       780
CCC
                                                                       783
      <210> 16
      <211> 801
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(801)
      <223> n = A,T,C or G
      <400> 16
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa
                                                                        60
agetgattga ageaaceete taetttttgg tegtgageet tttgettggt geaggtttea
                                                                       120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg
                                                                       180
aagtagggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc
                                                                       240
atggtggtgt tccacacttg agtgaagtct tcctggggaac cataatcttt cttgatggca
                                                                       300
ggcactacca gcaacgtcag gaagtgctca gccattgtgg tgtacaccaa ggcqaccaca
                                                                       360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncqagggca
                                                                       420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg
                                                                       480
cengetgega atgaaagaaa ntacccaegt tgacaaactg catggccact ggacgacagt
                                                                      540
tggcccgaan atcttcagaa aagggatgcc ccatcgattg aacacccana tgcccactgc
                                                                       600
cnacagggct gencenenen gaaagaatga gecattgaag aaggatente ntggtettaa
                                                                       660
tgaactgaaa centgeatgg tggeeeetgt teagggetet tggeagtgaa ttetganaaa
                                                                      720
aaggaacngc ntnagccccc ccaaangana aaacaccccc gggtgttgcc ctgaattqqc
                                                                      780
ggccaaggan ccctgccccn g
                                                                       801
      <210> 17
      <211> 740
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(740)
      <223> n = A,T,C or G
      <400> 17
gtgagagcca ggcgtccctc tgcctgccca ctcagtggca acacccggga gctgttttgt
                                                                        60
```

300

```
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaaqagc cctqaacaqq
                                                                        120
agccaccatg cagtgcttca gcttcattaa gaccatgatg atcctcttca atttgctcat
                                                                        180
ctttctqtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc
                                                                        240
ctttctqaaq atcttcqqqc cactqtcqtc caqtqccatq caqtttqtca acqtqqqcta
                                                                        300
cttcctcatc qcaqccggcg ttgtggtctt tgctcttggt ttcctqqqct qctatqqtqc
                                                                       360
taagacqqaq aqcaaqtqtq ccctcqtqac qttcttcttc atcctcctcc tcatcttcat
                                                                        420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatqqctq aaccattcct
                                                                        480
gacgttgctg gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc
                                                                        540
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccq
                                                                        600
gaattttgaa aganteneee taetteeaaa aaaaaanant tgeetttnee eeenttetgt
                                                                        660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa
                                                                        720
caaaaaant nnaagggttn
                                                                        740
      <210> 18
      <211> 802
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(802)
      <223> n = A,T,C \text{ or } G
      <400> 18
ccgctggttg cgctggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca
                                                                        60
caaggtette cagetgeege acattaegea gggeaagage etecageaac actgeatatg
                                                                       120
ggatacactt tactttagca gccagggtga caactgagag gtgtcgaagc ttattcttct
                                                                       180
gagcctctgt tagtggagga agattccggg cttcagctaa gtagtcagcg tatgtcccat
                                                                       240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa
                                                                       300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnqqcctcc aqcacctqat
                                                                       360
qqatqaqtqt qqccaqcqct qcccccttqq ccqacttqqc taqqaqcaqa aattqctcct
                                                                       420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttqq
                                                                       480
getcaggatg tecagagacg tggttcegee cectenetta atgacaceqn ceanneaace
                                                                       540
gteggeteee geegantgng ttegtegtne etgggteagg gtetgetgge enetaettge
                                                                       600
aancttegte nggeecatgg aatteacene aceggaactn gtangateea etnnttetat
                                                                       660
aaccggncgc caccgcnnnt ggaactccac tcttnttncc tttacttgag ggttaaggtc
                                                                       720
accettnincy tracettggt ccaaacentn centgtgteg anatngtnaa tengqneena
                                                                       780
tnccancene atangaagee ng
                                                                       802
      <210> 19
      <211> 731
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(731)
      \langle 223 \rangle n = A,T,C or G
      <400> 19
chaagettee aggtnaeggg cegenaanee tgaeeenagg tancanaang cagnengegg
                                                                        60
gagcccaccg tcacgnggng gngtctttat nggaggggc ggagccacat cnctggacnt
                                                                       120
cntgacccca actccccncc nencantgca gtgatgagtq caqaactqaa qqtnacqtqq
                                                                       180
caggaaccaa gancaaanne tgeteennte caagteggen nagggggegg ggetggeeae
                                                                       240
```

geneateent enagtgetgn aaageeeenn eetgtetaet tgtttggaga aengennnga

```
catgeccagn gttanataac nggengagag tnantttgee tetecettee ggetgegean
                                                                        360
cgngtntgct tagnggacat aacctgacta cttaactgaa cccnngaatc tnccnccct
                                                                        420
ccactaaget cagaacaaaa aacttegaca ccacteantt gteacetgne tgeteaagta
                                                                        480
aagtgtaccc catneccaat gtntgetnga ngetetgnee tgenttangt teggteetgg
                                                                        540
gaagacctat caattnaagc tatgtttetg actgeetett geteeetgna acaanenace
                                                                        600
ennennteca aggggggne ggccccaat cccccaacc ntnaattnan tttancccn
                                                                        660
ecceenggee eggeetttta enanentenn nnaengggna aaacennnge tttneccaae
                                                                        720
nnaatccncc t
                                                                        731
      <210> 20
      <211> 754
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(754)
      <223> n = A, T, C \text{ or } G
      <400> 20
ttttttttt tttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc
                                                                        60
caaccccctc ntccaaatnn ccntttccgg gngggggttc caaacccaan ttanntttgg
                                                                       120
annttaaatt aaatnttnnt tggnggnnna anccnaatgt nangaaagtt naacccanta
                                                                       180
tnancttnaa tncctggaaa congtngntt ccaaaaatnt ttaaccctta antccctccg
                                                                       240
aaatngttna nggaaaaccc aanttctcnt aaggttgttt gaaggntnaa tnaaaanccc
                                                                       300
nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa
                                                                       360
ggnnancece ggttantnaa teeceeenne eecaattata eeganttitt tingaattgg
                                                                       420
ganccenegg gaattaacgg ggnnnnteec tnttgggggg enggnneece eccenteggg
                                                                       480
ggttngggnc aggncnnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc
                                                                       540
ccaggntgag nntngggttt ncccccccc canggcccct ctcgnanagt tggggtttgg
                                                                       600
ggggcctggg attttntttc ccctnttncc tcccccccc ccnggganag aggttngngt
                                                                       660
tttgntcnnc ggccccnccn aaganctttn ccganttnan ttaaatccnt gcctnggcga
                                                                       720
agtccnttgn agggntaaan ggccccctnn cggg
                                                                       754
      <210> 21
      <211> 755
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(755).
      <223> n = A, T, C or G
      <400> 21
atcancecat gacceenaac nngggacene teaneeggne nnnenacene eggeenatea
                                                                        60
nngtnagnnc actnennttn natcaencee encenactae gecenenane enaegeneta
                                                                       120
nncanatnee actganngeg egangtngan ngagaaanet nataccanag neaccanaen
                                                                       180
ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn
                                                                       240
nncnncanat gatttteetn anecgattae centneecce taneccetee eccecaaena
                                                                       300
cgaaggenet ggneenaagg nngegnenee eegetagnte eeenneaagt eneneneeta
                                                                       360
aactcancen nattacnege ttentgagta teacteeeeg aateteacee tactcaacte
                                                                       420
aaaaanatcn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt
                                                                       480
tragnggtcc ntnaanchtc ctaatacttc cagtctncct tcnccaattt ccnaanggct
                                                                       540
ctttengaea geathttttg gtteeenntt gggttettan ngaattgeee ttentngaae
                                                                      600
```

```
gggetentet titeettegg tianeetggn tienneegge eagitatiat tieeentitt
                                                                        660
aaattentne entttanttt tggenttena aaceeegge ettgaaaaeg geeeeetggt
                                                                        720
aaaaggttgt tttganaaaa tttttgtttt gttcc
                                                                        755
      <210> 22
      <211> 849
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(849)
      <223> n = A,T,C or G
      <400> 22
tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt
                                                                        60
acgetnggan taangegace eganttetag ganneneeet aaaateanae tgtgaagatn
                                                                       120
atcetgnnna eggaanggte aceggnngat nntgetaggg tgncenetee cannnenttn
                                                                       180
cataacteng nggccctgcc caccacette ggcggcccng ngnccgggcc cgggtcattn
                                                                       240
qnnttaaccn cactnngcna neggttteen neecenneng accenggega teeggggtne
                                                                       300
tetgtettee eetgnagnen anaaantggg eeneggneee etttaceeet nnacaageea
                                                                       360
engeenteta neenengeee eeceteeant nngggggaet geenannget eegttnetng
                                                                       420
nnaccconnn gggtncctcg gttgtcgant cnaccgnang ccanggattc cnaaggaagg
                                                                       480
tgcgttnttg gcccctaccc ttcgctncgg nncacccttc ccgacnanga nccgctcccg
                                                                       540
enennegning cetenecteg caacaceege netentengt neggninece ecceaceege
                                                                       600
necetenene ngnegnanen eteeneenee gteteannea ecaeceegee eegeeaggee
                                                                       660
nteanceaen ggnngaenng nagenennte geneegegen gegneneeet egeenengaa
                                                                       720
ctnentengg ccantinge teaaneenna enaaaegeeg etgegegee egnagegnee
                                                                       780
necteenega gteeteeegn etteenaeee angnntteen egaggaeaen nnaeeeegee
                                                                       840
nncangcgg
                                                                       849
      <210> 23
      <211> 872
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(872)
      \langle 223 \rangle n = A,T,C or G
      <400> 23
gegeaaacta tacttegete gnactegtge geetegetne tetttteete egeaaceatg
                                                                        60
totgacnano cogattnggo ngatatonan aagntogano agtocaaact gantaacaca
                                                                       120
cacaenenan aganaaatee netgeettee anagtanaen attgaaenng agaaeeange
                                                                       180
nggcgaatcg taatnaggcg tgcgccgcca atntgtcncc gtttattntn ccagcntcnc
                                                                       240
ctnccnaccc tacntcttcn nagetgtcnn acccctngtn cgnacccccc naggtcqqqa
                                                                       300
tegggtttnn nntgacegng enneceetee eccentecat nacganeene eegeaceaee
                                                                       360
nanngenege neceegnnet ettegeenee etgteetntn eeeetgtnge etggenengn
                                                                       420
accgcattga ccctcgccnn ctncnngaaa ncgnanacgt ccgggttgnn annancgctg
                                                                       480
tgggnnngcg tetgeneege gtteetteen nennetteea ecatettent taengggtet
                                                                       540
conegeente tennneache cetgggaege intectnige ecceetinae tecceeceti
                                                                       600
egnegtgnee egneceeace nteattinea nacgniette acaannneet ggninnetee
                                                                       660
cnancngncn gtcanccnag ggaagggngg ggnnccnntg nttgacgttg nggngangtc
                                                                      720
cgaanantcc tencentean enctaceeet egggegnnet etengttnee aaettaneaa
                                                                      780
```

```
840
ntctccccq ngngenentc tcagcctenc cencecenet ctetgcantg tnctctgctc
tnaccnntac gantnttcgn enecetettt ee
                                                                       872
      <210> 24
      <211> 815
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(815)
      <223> n = A, T, C \text{ or } G
      <400> 24
qcatqcaaqc ttqaqtattc tataqqqtca cctaaatanc ttqqcntaat catqqtcnta
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nctqncttcc tgtgtcaaat gtatacnaan tanatatgaa tctnatntga caaganngta
                                                                       120
tentneatta gtaacaantg tnntgteeat eetgtengan canatteeca tnnattnegn
                                                                       180
cgcattenen geneantatn taatngggaa ntennntnnn neacenneat etatentnee
                                                                       240
qcnccctqac tggnaqagat ggatnanttc tnntntgacc nacatgttca tcttggattn
                                                                       300
aananceece egengneeae eggtingning enageennie eeaagaeete etgiggaggt
                                                                       360
aacctgcgtc aganncatca aacntgggaa acccgcnncc angtnnaagt ngnnncanan
                                                                       420
gatecegtee aggnttnace atceettene agegeeecet tingtgeett anagngnage
                                                                       480
gtgtccnanc cnctcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc
                                                                       540
gaacccccta gggggantna thcaaanccc caggattgtc chchcangaa atccchcanc
                                                                       600
ccencectae cennetttgg gaengtgaee aanteeegga gtneeagtee ggeengnete
                                                                       660
ccccaccggt nnccntgggg gggtgaanct cngnntcanc cngncgaggn ntcgnaagga
                                                                       720
accggnectn ggnegaanng anenntenga agngeenent egtataacce ecceteneca
                                                                       780
ncenacngnt agntcccccc engggtnegg aangg
                                                                       815
      <210> 25
      <211> 775
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(775)
      <223> n = A, T, C \text{ or } G
      <400> 25
eegagatgte tegeteegtg geettagetg tgetegeget actetetett tetggeetgg
                                                                        60
aggetateca gegtaeteca aagatteagg tttaeteaeg teateeagea gagaatggaa
                                                                       120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact
                                                                       180
tactqaaqaa tqqanaqaqa attgaaaaaag tggagcattc aqacttgtct ttcagcaagg
                                                                       240
actqqtcttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg
                                                                       300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca
                                                                       360
tgtaagcagn cnncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt
                                                                       420
ctgcttgctt gcnttttaat antgatatgc ntatacaccc taccctttat gnccccaaat
                                                                       480
tgtaggggtt acatnantgt tcncntngga catgatette etttataant cencentteg
                                                                       540
aattgcccgt enecengttn ngaatgttte ennaaceaeg gttggeteee eeaggtenee
                                                                       600
tettaeggaa gggeetggge enetttneaa ggttggggga acenaaaatt tenettntge
                                                                       660
conceneca enntettgng nnencanttt ggaaccette enatteeect tggeetenna
                                                                       720
nccttnncta anaaaacttn aaancgtngc naaanntttn acttccccc ttacc
                                                                       775
```

```
<211> 820
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(820)
       <223> n = A, T, C \text{ or } G
       <400> 26
 anattantac agtgtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat
                                                                         60
 cccanagata nettatanca acagtgettt gaccaagage tgetgggeae attteetgea
                                                                        120
 gaaaaggtgg cggtccccat cactcctcct ctcccatagc catcccagag gggtgagtag
                                                                        180
 ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca
                                                                        240
 ntgatgacca tgggcgggag cgagcctctt ccctgnaccg gggtggcana nganagccta
                                                                        300
 nctgagggt cacactataa acgttaacga conagatnan cacctgcttc aagtgcaccc
                                                                        360
 ttcctacctg acnaccagng accnnnaact gengeetggg gacagenetg ggancageta
                                                                        420
 acnnageact caectgeece cecatggeeg thegenteec tggteetgne aagggaaget
                                                                        480
 ccctqttqqa attncgggga naccaaggga nccccctcct ccanctgtga aggaaaaann
                                                                        540
 gatggaattt thecetteeg geennteece tetteettta eaegeeect nntactente
                                                                        600
 tecetetntt nteetquene aettttnace cennnattte cettnattga teggannetn
                                                                        660
 ganattecac thnequetne entenating maanachaaa macthtetna ceengggat
                                                                        720
 gggnncctcg nteatectet ettttenet accneenntt etttgeetet eettngatea
780tccaacente gntggeentn eececennn teetttneee
820
       <210> 27
       <211> 818
       <212> DNA
       <213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(818)
       \langle 223 \rangle n = A,T,C or G
 tetgggtgat ggeetettee teeteaggga cetetgactg etetgggeea aagaatetet
                                                                         60
 tgtttcttct ccgagcccca ggcagcggtg attcagccct gcccaacctg attctgatga
                                                                        120
 ctqcqqatqc tgtqacgqac ccaaggggca aatagggtcc cagggtccag ggaggggcgc
                                                                        180
 ctgctgagca cttccgcccc tcaccctgcc cageccctgc catgagctct gggctgggtc
                                                                        240
 teegeeteea gggttetget etteeangea ngeeaneaag tggegetggg ceacaetgge
                                                                        300
 ttetteetge ecentecetg getetgante tetgtettee tgteetgtge angeneettg
                                                                        360
 qatctcaqtt tecetenete anngaactet qtttetgann tetteantta actntgantt
                                                                        420
 tatnacenan tggnetgtne tgtennactt taatgggeen gaeeggetaa teeeteeete
                                                                        480
 nctcccttcc anttcnnnna accnqcttnc cntcntctcc ccntancccg ccnqqqaanc
                                                                        540
 ctectttqcc ctnaccangg gccnnnaccg cccntnnctn ggggggcnng gtnnctncnc
                                                                        600
 etgntnnece enetenennt theetegtee ennennegen nngeanntte nengteeenn
                                                                        660
 thnctcttcn ngthtcqnaa nghtchchtn thnnnnqnch nghtnnthch tccctctchc
                                                                        720
 connitroning tintinning neighbors nonnennin nggnintinn tetnenenge
                                                                        780
 ccennecece ngnattaagg ceteenntet eeggeene
                                                                        818
```

<210> 28

<211> 731

<212> DNA

```
<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(731)
      <223> n = A, T, C \text{ or } G
      <400> 28
aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg
                                                                         60
tececaacatg anggtgnngt tetettttga angagggttg ngtttttann eenggtgggt
                                                                        120
gattnaaccc cattgtatgg agnnaaaggn tttnagggat ttttcggctc ttatcagtat
                                                                        180
ntanattcct gtnaatcgga aaatnatntt tcnncnggaa aatnttgctc ccatccqnaa
                                                                        240
attnctcccg ggtagtgcat nttngggggn cngccangtt tcccaggctg ctanaatcgt
                                                                        300
actaaagntt naagtgggan tncaaatgaa aacctnncac agagnatccn tacccgactg
                                                                        360
tnnnttnect tegecetntg actetgenng ageceaatae cenngngnat gtenecengn
                                                                        420
nnngegnene tgaaannnne tegnggetnn gancateang gggtttegea teaaaagenn
                                                                        480
egitteneat naaggeactt ingesteate caaceneing ecetennesa ittingesque
                                                                        540
nggttenect acgetnning encetnnin ganattithe eegecingg naanceteet
                                                                        600
gnaatgggta gggncttntc ttttnaccnn gnggtntact aatcnnctnc acgcntnctt
                                                                        660
tetenacece ecceetttt caateeeane ggenaatggg gteteceenn eganggggg
                                                                        720
nnncccannc c
                                                                        731
      <210> 29
      <211> 822
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(822)
      <223> n = A, T, C \text{ or } G
      <400> 29
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                                                                        60
egeteanace teacaneete cenaenange etataangaa nannaataga netgtnennt
                                                                       120
aththtache teatannect ennnaceeae teeetettaa eeentaetgt geetatngen
                                                                       180
tnnctantct ntgccgcctn cnanccaccn gtgggccnac cncnngnatt ctcnatctcc
                                                                       240
tenecatnin gectananta ngineatace etatacetae necaaigeta nnnetaanen
                                                                       300
tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc
                                                                       360
tactctgact cccacngcct annnattagc anentecccc nacnatntct caaccaaatc
                                                                       420
ntcaacaacc tatctanctg ttcnccaacc nttncctccg atccccnnac aaccccctc
                                                                       480
ccaaataccc nccacctgac ncctaacccn caccatcccg gcaagccnan ggncatttan
                                                                       540
ccactggaat cacnatngga naaaaaaaac ccnaactctc tancncnnat ctccctaana
                                                                       600
aatneteetn naatttaetn neantneeat caaneecaen tgaaaennaa eeeetgtttt
                                                                       660
tanatecett etttegaaaa eenaceettt annneecaae etttngggee eeceenetne
                                                                       720
ccnaatgaag gneneceaat enangaaaeg neentgaaaa anenaggena anannnteeg
                                                                       780
canatectat ceettanttn ggggneeett neeengggee ee
                                                                       822
      <210> 30
      <211> 787
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
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<222> (1)...(787)
      \langle 223 \rangle n = A,T,C or G
      <400> 30
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                                                                         60
ctaqaqaaqa cettetetee tactgteatt atggageeet geagaetgag ggeteeeett
                                                                        120
qtctqcaqqa tttqatqtct qaaqtcqtqq aqtgtqqctt ggagctcctc atctacatna
                                                                        180
gctggaagec ctggagggc tctctcgcca gcctcccct tctctccacg ctctccangg
                                                                        240
acaccagggg ctccaggcag cccattattc ccagnangac atggtgtttc tccacgcgga
                                                                        300
cccatggggc ctgnaaggcc agggtctcct ttgacaccat ctctcccgtc ctgcctqca
                                                                        360
ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt
                                                                        420
tecenttaat qaaqqttaat tgenegettg gegtaateat nggteanaae tnttteetgt
                                                                        480
qtqaaattqt ttntcccctc ncnattccnc ncnacatacn aacccggaan cataaaqtqt
                                                                        540
taaaqcctqq qqqtnqcctn nngaatnaac tnaactcaat taattgcgtt ggctcatggc
                                                                        600
cogotttoon ttonggaaaa ctqtcntccc ctqcnttnnt qaatcqqcca cccccnqqq
                                                                        660
aaaaggggtt tgcnttttng ggggntcctt ccncttcccc cctcnctaan ccctncqcct
                                                                        720
cggtcgttnc nggtngcggg gaangggnat nnnctcccnc naagggggng agnnngntat
                                                                        780
ccccaaa
                                                                        787
      <210> 31
      <211> 799
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(799)
      \langle 223 \rangle n = A,T,C or G
      <400> 31
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                                                                         60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc
                                                                        120
aacaaaggac teetgeagee ttetetgtet gtetettgge geaggeacat ggggaggeet
                                                                        180
cccqcaqqqt qqqqqccacc aqtccaqqqq tqqqaqcact acanqqqqtq gqaqtqqqtq
                                                                        240
gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca
                                                                        300
qqqqacettc tqttetecca nqqnaacttc ntnnatcten aaagaacaca actqtttett
                                                                        360
engeanttet ggetgtteat ggaaageaca ggtgteenat ttnggetggg aettggtaca
                                                                        420
tatggtteeg geccaectet eeentenaan aagtaattea eeeeeeeen eentetnttg
                                                                        480
cctqqqccct taantaccca caccggaact canttantta ttcatcttng gntgggcttg
                                                                        540
ntnateneen eetgaangeg eeaagttgaa aggeeaegee gtneeenete eecatagnan
                                                                        600
nttttnnent canctaatge eeceeengge aacnateeaa teeceeecen tgggggeeee
                                                                        660
ageceange eccepneteg gennneengn enegnantee ecagentete ceantengne
                                                                        720
connegence ecegeacqca qaacanaagg ntngageene egeannennn nggtnnenae
                                                                        780
ctcgccccc ccnncgnng
                                                                        799
      <210> 32
      <211> 789
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(789)
      <223> n = A, T, C \text{ or } G
```

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```
<400> 32
60
ttttnccnag ggcaggttta ttgacaacct cncgggacac aancaggctg ggqacaqqac
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ggcaacaggc tecggeggeg geggeggegg cectacetge ggtaccaaat ntgcageete
                                                                      180
cgctcccgct tgatnttcct ctgcagctgc aggatgccnt aaaacagggc ctcggccntn
                                                                      240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc
                                                                      300
nattaggaat agtggtntta cocncenceg ttggcncact cocentggaa accacttnte
                                                                      360
geggeteegg catetggtet taaacettge aaacnetggg geeetetttt tggttantnt
                                                                      420
ncengecaca atcatnacte agactggene gggetggeee caaaaaanen eeccaaaace
                                                                      480
ggnccatgtc ttnncggggt tgctgcnatn tncatcacct cccgggcnca ncaggncaac
                                                                      540
ccaaaagttc ttgnggcccn caaaaaanct ccggggggnc ccagtttcaa caaagtcatc
                                                                      600
ccccttggcc cccaaatcct cccccgntt nctgggtttg ggaacccacg cctctnnctt
                                                                      660
tggnnggcaa gntggntccc ccttcgggcc cccggtgggc ccnnctctaa nqaaaacncc
                                                                      720
ntectnnnea ceatecece nngnnaegne tancaangna teeettttt tanaaaeggg
                                                                      780
cccccncg
                                                                      789
      <210> 33
      <211> 793
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(793)
      <223> n = A, T, C \text{ or } G
      <400> 33
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                                                                      60
aattcatggc tgttggagca atanaacccc agttctacga gctgctgatc aaaggacttg
                                                                     120
qactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana
                                                                     180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacq
                                                                     240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca
                                                                     300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac
                                                                     360
ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc
                                                                     420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct
                                                                     480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac
                                                                     540
acaacatacg anccggaagc atnaaatttt aaagcctggn ggtngcctaa tgantgaact
                                                                     600
nactcacatt aattggcttt gegetcactg ceegetttee agteeggaaa acetgteett
                                                                     660
gccagctgcc nttaatgaat cnggccaccc cccggggaaa aggcngtttg cttnttgggg
                                                                     720
egenetteec getttetege tteetgaant eetteecece ggtetttegg ettgeggena
                                                                     780
acggtatcna cct
                                                                     793
     <210> 34
     <211> 756
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(756)
     \langle 223 \rangle n = A,T,C or G
     <400> 34
gccgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaaq ccccaatctt
                                                                      60
ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctqqaqct caacttcttq
                                                                     120
```

```
ccaaccacaq ggaccaagct gaccaaacaq cagctaattc tqqccqtqa catactqqaq
                                                                       180
ateggggee aatggageat cetacgeaan gacateceet cettegageg etacatggee
                                                                       240
caqctcaaat qctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac
                                                                       300
caqctcttgg gcctcaacct cctcttcctg ctgtcccaga accgggtggc tgantnccac
                                                                       360
acgganttgg ancggctgcc tgcccaanga catacanacc aatgtctaca tcnaccacca
                                                                       420
gtgtcctgga gcaatactga tgganggcag ctaccncaaa qtnttcctqq ccnaqqqtaa
                                                                       480
catcccccgc cgagagetac accttettea ttgacatect getegacaet atcagggatg
                                                                       540
aaaategeng ggttgeteea gaaaggetne aanaanatee ttttenetga aggeeeegg
                                                                       600
athenetagt netagaateg geogecate geggtggane etceaacett tegttnecet
                                                                       660
ttactgaggg ttnattgccg cccttggcgt tatcatggtc acncengttn cctqtqttga
                                                                       720
aattnttaac cccccacaat tccacqccna cattng
                                                                       756
      <210> 35
      <211> 834
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(834)
      <223> n = A,T,C or G
      <400> 35
ggggatctct anatchacct gnatgcatgg ttgtcggtgt ggtcgctgtc gatgaanatg
                                                                        60
aacaggatet tgeeettgaa getetegget getgtnttta agttgeteag tetgeegtea
                                                                       120
tagtcagaca cnctcttggg caaaaaacan caggatntga gtcttgattt cacctccaat
                                                                       180
aatcttengg getgtetget eggtgaacte gatgaenang ggeagetggt tgtgtntqat
                                                                       240
aaantccanc angttctcct tggtgacctc cccttcaaag ttgttccggc cttcatcaaa
                                                                       300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactgtt
                                                                       360
ggaaactgat cccaaatggt atgtcatcca tcgcctctgc tgcctgcaaa aaacttqctt
                                                                       420
ggcncaaatc cgactccccn tccttgaaag aagccnatca cacccccctc cctggactcc
                                                                       480
nneaangaet etneegetne eeenteenng eagggttggt ggeanneegg geeentgege
                                                                       540
ttetteagee agtteaenat ntteateage ecetetgeea getgttntat teettqqqqq
                                                                       600
ggaanccgtc tctcccttcc tgaannaact ttgaccgtng gaatagccgc gcntcnccnt
                                                                       660
achtnetggg cegggtteaa anteceteen ttgnennten cetegggeea ttetqqattt
                                                                       720
nccnaacttt ttccttcccc cnccccncgg ngtttggntt tttcatnqqq ccccaactct
                                                                       780
gethttggcc anteceetgg gggenthtan enceceetht ggtecentng ggcc
                                                                       834
      <210> 36
      <211> 814
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(814)
      <223> n = A, T, C or G
      <400> 36
eggnegettt eengeegege eeegttteea tgacnaagge teeetteang ttaaataenn
                                                                        60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca
                                                                       120
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tqqtctctcc acccctqta
                                                                       180
ggaaaggcct gccttqtaaq acaccacaat ncqqctqaat ctnaaqtctt qtqttttact
                                                                       240
aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccq caqcctqqca
                                                                       300
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttqctctt ttqqacatca
                                                                       360
```

```
ggcttgatgg tatcactgcc acntttccac ccaqctqqqc ncccttcccc catntttqtc
                                                                       420
antganctgg aaggeetgaa nettagtete caaaagtete ngcccacaaq accqqccace
                                                                       480
aggggangtc ntttncagtg gatctgccaa anantacccn tatcatcnnt gaataaaaag
                                                                       540
gcccctgaac ganatgcttc cancancctt taagacccat aatcctngaa ccatggtgcc
                                                                       600
cttccqqtct gatccnaaag gaatgttcct gggtcccant ccctcctttg ttncttacqt
                                                                       660
tgtnttggac centgetngn atnacecaan tganatecec ngaaqeacec tnecectqge
                                                                       720
atttganttt chtaaattct ctgccctach nctgaaagca chattcccth ggchcchaan
                                                                       780
ggngaactca agaaggtctn ngaaaaacca cncn
                                                                       814
      <210> 37
      <211> 760
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(760)
      <223> n = A,T,C or G
      <400> 37
geatgetget etteeteaaa gttgttettg ttgccataac aaccaccata ggtaaagegg
                                                                        60
gcgcagtgtt cgctgaaggg gttgtagtac cagcgcggga tgctctcctt qcaqaqtcct
                                                                       120
gtgtctggca ggtccacgca atgccctttg tcactgggga aatggatgcg ctggagctcg
                                                                       180
tenaaneeae tegtgtattt tteacangea geeteeteeg aagenteegg geagttgggg
                                                                       240
gtgtcgtcac actccactaa actgtcgatn cancagecca ttgctgcage ggaactgggt
                                                                       300
gggctgacag gtgccagaac acactggatn ggcctttcca tggaaqqqcc tqqqqqaaat
                                                                       360
encetnance caaactgeet etcaaaggee acettgeaca eccegacagg etagaaatge
                                                                       420
actettette ccaaaggtag ttgttettgt tgeecaagea neeteeanea aaceaaaane
                                                                       480
ttgcaaaatc tgctccgtgg gggtcatnnn taccanggtt ggggaaanaa acccqqcnqn
                                                                       540
ganceneett gtttgaatge naaggnaata ateeteetgt ettgettggg tggaanagea
                                                                      600
caattgaact gttaacnttg ggccgngtte enetngggtg gtctgaaact aatcaccgte
                                                                      660
actggaaaaa ggtangtgcc ttccttgaat tcccaaantt cccctnqntt tqqqtnnttt
                                                                      720
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      <211> 724
      <212> DNA
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      <220>
      <221> misc feature
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      <223> n = A,T,C or G
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                                                                      120
caaattaatt ttgganttta aattaaatnt tnattngggg aanaanccaa atgtnaagaa
                                                                      180
aatttaaccc attatnaact taaatneetn gaaaccentg gntteeaaaa atttttaacc
                                                                      240
cttaaatccc tccgaaattg ntaanggaaa accaaattcn cctaaqqctn tttqaaqqtt
                                                                      300
ngatttaaac coccttnant tnttttnacc cnngnctnaa ntatttngnt tooggtgttt
                                                                      360
tectnttaan entnggtaac teeegntaat gaanneeet aaneeaatta aaceqaattt
                                                                      420
tttttgaatt ggaaattcon ngggaattna coqqqqtttt tocontttgg qqqccatnco
                                                                      480
ccencttteg gggtttgggn ntaggttgaa tttttnnang neceaaaaaa nececeaana
                                                                      540
aaaaaactcc caagnnttaa ttngaatntc ccccttccca qqccttttqq qaaaqqnqqq
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tttntggggg congggantt onttocccon ttnconccc coccconggt aaanqqttat
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ngnntttggt tittgggeee ettnanggae etteeggain gaaattaaat eecegggneg
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                                                                       724
gccg
      <210> 39
      <211> 751
      <212> DNA
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      <220>
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                                                                       120
tttatttatt tttactgaaa gtgagaggga acttttgtgg ccttttttcc ttttctgta
                                                                       180
qqccqcctta agctttctaa atttggaaca tctaagcaag ctgaanggaa aagggggttt
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cqcaaaatca ctcgggggaa nggaaaggtt gctttgttaa tcatgcccta tggtgggtga
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ttaactqctt qtacaattac ntttcacttt taattaattg tgctnaangc tttaattana
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cttgggggtt ccctccccan accaaccccn ctgacaaaaa gtgccngccc tcaaatnatg
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teceggennt entigaaaca eaengengaa ngiteteatt nieceenene eagginaaaa
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tqaagggtta ccatntttaa cnccacctcc acntggcnnn gcctgaatcc tcnaaaancn
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coctcaanon aattnotning coccggtone gentingtoe eneceggget cogggaantin
                                                                       600
caccconga annonnthno naacnaaatt cogaaaatat toocnntono toaattooco
                                                                       660
                                                                       720
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nnnnencete enetngteen naateneean e
                                                                       751
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      <211> 753
      <212> DNA
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      <220>
      <221> misc_feature
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                                                                       120
eqecetatge acagetggge cettgagaea geagggette gatgteagge tegatgteaa
                                                                       180
tggtctggaa gcggcggctg tacctgcgta ggggcacacc gtcagggccc accaggaact
                                                                       240
teteaaagtt eeaggeaaen tegttgegae acaeeggaga eeaggtgatn agettggggt
                                                                       300
eggteataan egeggtegeg tegtegeteg gagetegeag ggeeteeege aggaaggena
                                                                       360
ataaaaggtg cgccccgca ccgttcanct cgcacttctc naanaccatg angttgggct
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enaacceacc accanneegg actteettga nggaatteec aaatetette gntettggge
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ttctnctqat qccctanctq qttqcccnqn atqccaanca nccccaancc ccqqqqtcct
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aaancaccon cetectentt teatetgggt tnttnteece ggacentggt teeteteaag
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qqancccata tetenacean tacteacent neceeecent gnnacecane ettetanngn
                                                                       660
tteceneceq neetetggee enteaaanan gettneacna eetgggtetg eetteeeeee
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tnecetatet gnacecenen tttgtetean tnt
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                                                                       120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt
                                                                       180
tatagettgt ttacgtagta agtttttqaa qtctacattc aatccaqaca cttagttgag
                                                                       240
tgttaaactg tgatttttaa aaaatatcat ttgagaatat tctttcaqaq qtattttcat
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      <212> DNA
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gtttcaaaca ttctaaataa ataattttca gtggcttcat a
                                                                       101
      <210> 43
      <211> 305
      <212> DNA
      <213> Homo sapien
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tccagggtgg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat
                                                                       120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca
                                                                       180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat
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tcgaa
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      <211> 852
      <212> DNA
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      <221> misc_feature
      <222> (1)...(852)
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gattattigg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt
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ctctccatcc togggcattc ttcccaaatt tatataccag tcttcqtcca tccacacqct
                                                                      180
ccagaatttc tcttttgtag taatatctca tagctcggct gagcttttca tagqtcatqc
                                                                      240
tgctgttgtt cttctttta ccccatagct gagccactgc ctctgatttc aagaacctqa
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agacgccctc agatcggtct tcccatttta ttaatcctgg gttcttgtct qqqttcaaqa
                                                                      360
ggatgtcqcg gatgaattcc cataagtgag tccctctcgg gttgtgcttt ttggtgtqqc
                                                                      420
acttggcagg ggggtcttgc tcctttttca tatcaggtga ctctgcaaca qqaaqqtqac
                                                                      480
tggtggttgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg
                                                                      540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccaggtgttc atgatqqaaq
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geteagtttg tteagtettg acaatgaeat tgtgtgtgga etggaaeagg teactaetge
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                                                                       720
ccgcccgggt gaactcctgc aaactcatgc tgcaaaggtg ctcgccgttg atgtcgaact
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cntggaaagg gatacaattg gcatccagct ggttggtgtc caqqaqqtqa tqqaqccact
                                                                       840
cccacacctg gt
                                                                       852
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      <211> 234
      <212> DNA
      <213> Homo sapien
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geotegitte tggetggggt etgetggega aeggeagaat geetaeegtg etgeagtgeg
                                                                       180
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      <210> 46
      <211> 590
      <212> DNA
      <213> Homo sapien
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      <221> misc feature
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      <223> n = A,T,C or G
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atttgatagc aatattttgg agattacaga gttttagtaa ttaccaatta cacaqttaaa
                                                                      120
aagaagataa tatattccaa gcanatacaa aatatctaat gaaagatcaa gqcaqqaaaa
                                                                      180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatccttta
                                                                      240
aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatqqtat
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caggataaan aactgaaggg canaaagaat taattttcac ttcatgtaac ncacccanat
                                                                      360
ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc
                                                                      420
tggtctctaa tctgccttac tctttgggtg tggctttgat cctctqqaqa caqctqccaq
                                                                      480
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct
                                                                      540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt
                                                                      590
      <210> 47
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      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      <223> n = A,T,C or G
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tgaacagaat tttcctgnac aacggggctt caaaataatt ttcttgggga ggttcaagac
                                                                      120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctqtaatg accctqaqqq
                                                                      180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa
                                                                      240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggctct
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cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctcctgtgtg
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ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc
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ccacacteet tgaacacaca tecceaggtt atatteetgg acatggetga aceteetatt
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cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc
                                                                         540
acggcatggg aagcetttet gacttgcctg attactccag catcttggaa caatccctga
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ttccccactc cttagaggca agatagggtg gttaagagta gggctggacc acttggagcc
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aggetgetgg etteaaattn tggeteattt acgagetatg ggaeettggg caagtnatet
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      <211> 124
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(124)
      <223> n = A,T,C \text{ or } G
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                                                                        120
tggt
                                                                        124
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      <211> 147
      <212> DNA
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      <221> misc feature
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      \langle 223 \rangle n = A,T,C or G
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tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt
                                                                        120
ttagggcacc catatcccaa gcantgt
                                                                        147
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      <211> 107
      <212> DNA
      <213> Homo sapien
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atggtttgag gttaggagga gttaggcata tgttttggga gaggggt
                                                                        107
      <210> 51
      <211> 204
      <212> DNA
      <213> Homo sapien
      <400> 51
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                                                                       60
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cgggaaggaa aggcagagaa gtgacaccgt gccttgcaag gtcagaaagg ggactcaggg cctccctttt gggaccagca atgt				120 180 204
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gccctccagt ggatactcga gccaaagtgg t
                                                                          91
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      <211> 133
      <212> DNA
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aagggacaac tgt
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gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana
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tctcantggg ctggatncat gcagggt
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      <211> 198
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(198)
      \langle 223 \rangle n = A,T,C or G
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tgattacata catttatcct ttaaaaaaga tgtaaatctt aatttttatg ccatctatta
                                                                        120
atttaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt
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ttgacttcta agtttggt
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      <210> 59
      <211> 330
      <212> DNA
      <213> Homo sapien
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<210> 64 <211> 97 <212> DNA <213> Homo sapien	
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      <212> DNA
      <213> Homo sapien
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      <221> misc_feature
      <222> (1)...(377)
      \langle 223 \rangle n = A,T,C or G
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ccaaccetgg tetacceaca nttetggeta tgggetgtet etgecaetga acateaqggt
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toggtcataa natqaaatoo caanggqqao agaggtcagt agaggaagot caatgagaaa
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qqtqctqttt qctcaqccaq aaaacaqctq cctqqcattc qccqctqaac tatqaacccq
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tqqqqqtqaa ctaccccan qagqaatcat qcctgggcga tgcaanggtg ccaacaqqaq
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gggcgggagg agcatgt
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      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 66
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agaaccegtg tgccccttcc caccatatcc accetegete catctttgaa ctcaaacacg
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aggaactaac tgcaccetgg teeteteece agteceeagt teacceteea teecteacet
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tectecacte taagggatat caacactgee cageacaggg geeetgaatt tatgtggttt
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ttatatattt tttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac
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tgttt
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      <211> 385
      <212> DNA
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                                                                       120
cccttttaaa aaaqqqqact tqcttaaaaa agaaqtctaq ccacqattqt qtaqaqcaqc
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tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg
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ctgggcaqtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctqcttg
                                                                       300
ceteteceag ggeeceagee tggeeacace tgettacagg geacteteag atgeceatac
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catagtttct gtgctagtgg accgt
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      <210> 68
      <211> 73
      <212> DNA
      <213> Homo sapien
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gtttttttaa tgg
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<210> 69
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      <212> DNA
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      <221> misc_feature
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      <223> n = A, T, C \text{ or } G
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cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat
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cccqqqtggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt
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cgccatcagc gagtataaca aggccaccaa agatgactac tacagacgtc cgctqcqqqt
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actaagagcc aggcaacaga ccgttggggg ggtgaattac ttcttcgacg tagaggtggg
                                                                       360
ccgaaccata tgtaccaagt cccagcccaa cttggacacc tgtgccttcc atgaacagcc
                                                                       420
agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagttccct qqqqaqaaca
                                                                       480
qaanqtccct gggtgaaatc caggtgtcaa gaaatcctan qqatctqttq ccaqqc
                                                                       536
      <210> 70
      <211> 477
      <212> DNA
      <213> Homo sapien
     <400> 70
atgacceta acaggggee teteageest cetaatgace teeggeetag ceatgtgatt
                                                                        60
teacttecae tecataaege teeteataet aggeetaeta accaacaea taaccatata
                                                                       120
ccaatqatqq cqcqatqtaa cacqaqaaaq cacataccaa qqccaccaca caccacctqt
                                                                       180
ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcqc
                                                                       240
agggattttt ctgagccttt taccactcca gcctagcccc tacccccaa ctaggagggc
                                                                       300
actggcccc aacaggcate accccgctaa atcccctaga agtcccactc ctaaacacat
                                                                       360
ccgtattact cgcatcagga gtatcaatca cctgagctca ccatagtcta atagaaaaca
                                                                       420
accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctatttt
                                                                       477
      <210> 71
      <211> 533
      <212> DNA
     <213> Homo sapien
      <220>
     <221> misc_feature
     <222> (1)...(533)
     \langle 223 \rangle n = A,T,C or G
      <400> 71
agagetatag gtacagtgtg ateteagett tgcaaacaca ttttetacat agatagtact
                                                                        60
aggtattaat agatatgtaa agaaagaaat cacaccatta ataatqqtaa qattqqttta
                                                                       120
tgtgatttta gtggtatttt tggcaccctt atatatgttt tccaaacttt cagcagtgat
                                                                       180
attatttcca taacttaaaa agtgagtttg aaaaagaaaa tctccagcaa gcatctcatt
                                                                       240
taaataaagg tttgtcatct ttaaaaatac agcaatatgt gactttttaa aaaagctgtc
                                                                       300
aaataggtgt gaccctacta ataattatta gaaatacatt taaaaacatc gagtacctca
                                                                       360
agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg
                                                                       420
cttcgtaatt ttggagtang aggttccctc ctcaattttg tatttttaaa aagtacatgg
                                                                       480
taaaaaaaaa aattcacaac agtatataag gctgtaaaat gaagaattct gcc
                                                                       533
```

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<210> 72
     <211> 511
      <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(511)
     \langle 223 \rangle n = A,T,C or G
     <400> 72
tattacqqaa aaacacacca cataattcaa ctancaaaqa anactqcttc aqqqcqtqta
                                                                      60
aaatqaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa
                                                                     120
aaqccqcaqq atqtctacac tatancaggc gctatttggg ttqqctqqaq qaqctqtqqa
                                                                     180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt
                                                                     240
gaggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca
                                                                     300
cacatgagaa ctgaaatggc ccaaacccag aaagaaagcc caactagatc ctcagaanac
                                                                     360
qcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgccccc gtctqttatg
                                                                     420
atttctctcc attqcaqcna naaacccqtt cttctaaqca aacncaqqtq atqatqqcna
                                                                     480
aaatacaccc cctcttgaag naccnggagg a
                                                                     511
     <210> 73
     <211> 499
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(499)
     \langle 223 \rangle n = A,T,C or G
     <400> 73
cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgcca gtgccagcac
                                                                      60
cagtggtggc ttcagtgctg gtgccagcct gaccgccact ctcacatttg ggctcttcgc
                                                                     120
tggccttggt ggagctggtg ccagcaccag tggcagctct ggtgcctgtg gtttctccta
                                                                     180
caagtgagat titagatatt gitaatcctg ccagtctttc tottcaagcc agggtgcatc
                                                                     240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca
                                                                     300
360
antetagagg gecegtttaa accegetgat cageetegae tgtgeettet anttgecage
                                                                     420
catctgttgt ttgcccctcc cccgntgcct tccttgaccc tggaaagtgc cactcccact
                                                                     480
gtcctttcct aantaaaat
                                                                     499
     <210> 74
      <211> 537
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1)...(537)
     <223> n = A,T,C or G
tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat
                                                                      60
```

```
ttatcagett aactcagata aaatcattga aagtaataag gtaaaageta gtetetaact
                                                                       120
tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa
                                                                       180
cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga
                                                                       240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaaatgg taatcattag
                                                                       300
ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc
                                                                       360
cagtitigett gatatatitig tigatatiaa gattetigae tiatatititig aaigggitet
                                                                       420
actgaaaaan gaatgatata ttottgaaga catogatata catttattta cactottgat
                                                                       480
tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccgt
                                                                       537
      <210> 75
      <211> 467
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(467)
      \langle 223 \rangle n = A,T,C or G
      <400> 75
caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc
                                                                        60
tgcatattac acgtacetec teetgeteet caagtagtgt ggtetatttt gecateatea
                                                                       120
cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg
                                                                       180
tggcacaagg aggccatctt ttcctcatcg gttattgtcc ctagaagcgt cttctgagga
                                                                       240
totagttggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta
                                                                       300
tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa
                                                                       360
caatgaggaa tagccacggt gatctccagc accaaatctc tccatgttnt tccagagctc
                                                                       420
ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn
                                                                       467
      <210> 76
      <211> 400
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(400)
      \langle 223 \rangle n = A,T,C or G
      <400> 76
aagetgacag cattegggee gagatgtete geteegtgge ettagetgtg etegegetae
                                                                        60
tetetette tggeetggag getateeage gtaeteeaaa gatteaggtt taeteaegte
                                                                       120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat
                                                                       180
ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag
                                                                       240
acttgtcttt cagcaaggac tggtctttct atctcttgta ctacactgaa ttcacccca
                                                                       300
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng
                                                                       360
ttnagtggga tcganacatg taagcagcan catgggaggt
                                                                       400
      <210> 77
      <211> 248
      <212> DNA
      <213> Homo sapien
      <400> 77
                                                                        60
etggagtgcc ttggtgtttc.aagcccctgc aggaagcaga atgcaccttc tgaggcacct
```

1

```
ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattqctqc
                                                                        120
caggeactgt teateteage tittetgice etitigeteec ggeaageget tetgetgaaa
                                                                        180
qttcatatct ggagcctgat gtcttaacga ataaaggtcc catgctccac ccgaaaaaaa
                                                                        240
aaaaaaaa
                                                                        248
      <210> 78
      <211> 201
      <212> DNA
      <213> Homo sapien
      <400> 78
actagtocag tgtggtggaa ttocattgtg ttgggcccaa cacaatggct acctttaaca
                                                                         60
tcacceagae ecegecetge eegtgeecea egetgetget aaegaeagta tqatqettae
                                                                        120
totgotacto ggaaactatt titatgiaat taatgiatgo titotigitt ataaatgoot
                                                                        180
gatttaaaaa aaaaaaaaaa a
                                                                        201
      <210> 79
      <211> 552
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(552)
      <223> n = A, T, C \text{ or } G
      <400> 79
teettttgtt aggtttttga gacaacccta gacctaaact gtgtcacaga ettetqaatq
                                                                         60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt
                                                                        120
cctctttctt ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag
                                                                        180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt
                                                                        240
atgeaagtta gtaattactc agggttaact aaattacttt aatatgetgt tqaacctact
                                                                        300
ctgttccttq gctaqaaaaa attataaaca ggactttgtt agtttqqqaa gccaaattqa
                                                                        360
taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta
                                                                        420
ttcccaggaa tatggggttc atttatgaat antacccggg anagaagttt tgantnaaac
                                                                        480
cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa
                                                                        540
aaaaaaaaa aa
                                                                        552
      <210> 80
      <211> 476
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(476)
      <223> n = A,T,C \text{ or } G
      <400> 80
acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga
                                                                         6.0
ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct
                                                                        120
cacacagact ceegagtage tgggactaca ggeacacagt cactgaagca ggeeetgttt
                                                                        180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta
                                                                        240
aggitaaact ticccaccca gaaaaggcaa citagataaa atcitagagt actiticatac
                                                                        300
tettetaagt cetetteeag ceteaetttg agteeteett gggggttgat aggaantnte
                                                                        360
```

```
tettggettt eteaataaaa tetetateea teteatgttt aatttggtae gentaaaaat
                                                                        420
gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaaa aaaaaaaaa aaaaaa
                                                                        476
      <210> 81
      <211> 232
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(232)
      <223> n = A, T, C \text{ or } G
      <400> 81
tttttttttt tatgcenten etgtggngtt attgttgetg ceaccetgga ggageceaqt
                                                                        60
ttettetgta tetttettt etgggggate tteetggete tgeceeteea tteecageet
                                                                       120
ctcatcccca tcttgcactt ttgctagggt tggaggcgct ttcctggtag cccctcagaq
                                                                       180
actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct
                                                                        232
      <210> 82
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(383)
      <223> n = A, T, C or G
      <400> 82
aggogggage agaagetaaa gecaaageee aagaagagty geagtgeeag cactgqtqee
                                                                        60
agtaccagta ccaataacat gccagtgcca gtgccagcac cagtggtqqc ttcaqtqctq
                                                                       120
gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggt ggagctggtg
                                                                       180
ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt
                                                                       240
gttaatcctg ccagtctttc tcttcaagcc agggtgcatc ctcagaaacc tactcaacac
                                                                       300
ageacteing geageeacta teaateaatt gaagttgaca etetgeatta aatetattig
                                                                       360
ccatttcaaa aaaaaaaaaa aaa
                                                                       383
      <210> 83
      <211> 494
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(494)
      <223> n = A,T,C or G
      <400> 83
accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca
                                                                        60
gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgctcagc
                                                                       120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaaqaa
                                                                       180
acgetteaag gtgeteatga cecageaace gegeeetgte etetqaqqqt cettaaactq
                                                                       240
atgtetttte tgecacetgt tacceetegg agaeteegta accaaactet teggaetgtg
                                                                       300
agccctgatg cettititged agccatacte titiggenice agtetetegt ggegatiqat
                                                                       360
```

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tatgcttgtg tgaggcaatc atggtggcat cacccatnaa gggaacacat ttganttttt
                                                                        420
tttcncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta
                                                                        480
aaaaaaaaa aaaa
                                                                        494
      <210> 84
      <211> 380
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(380)
      <223> n = A, T, C \text{ or } G
      <400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca
                                                                         60
agtatectge geogegicti ctacegicee tacetgeaga tettegggea gatteceeag
                                                                        120
. gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg
                                                                        180
gcacaccete etggggecca ggegggeace tgegtetece agtatgecaa etggetggtg
                                                                        240
gtgctgctcc togtcatctt cctgctcgtg gccaacatcc tgctgqtcac ttqctcattq
                                                                        300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc
                                                                        360
agcgttnccg cctcatccgg
                                                                        380
      <210> 85
      <211> 481
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(481)
      \langle 223 \rangle n = A,T,C or G
      <400> 85
gagttagete etecacaace ttgatgaggt egtetgeagt ggeetetege tteatacege
                                                                        60
tnccatcgtc atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca
                                                                       120
ggaaactete aatcaagtea eegtenatna aacetgtgge tggttetgte tteegetegg
                                                                       180
tgtgaaagga tetecagaag gagtgetega tetteceeae aettttgatg aetttattga
                                                                       240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc
                                                                       300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggt gnagtctcac
                                                                       360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa
                                                                       420
aaagaacacc tcctggaagt gctngccgct cctcgtccnt tggtggnngc gcntnccttt
                                                                       480
                                                                       481
      <210> 86
      <211> 472
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(472)
      <223> n = A,T,C or G
      <400> 86
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aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttqtctqctq aqaattcatt
                                                                         60
actiggaaaa gcaactinaa gcciqqacac tqqtattaaa attcacaata tqcaacacti
                                                                        120
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg
                                                                        180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga
                                                                        240
cacaagtccq aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt
                                                                        300
catgggacag agccatttga tttaaaaaagc aaattgcata atattgaqct ttqqqaqctq
                                                                        360
atatntgage ggaagantag cetttetaet teaceagaea caacteettt catattggga
                                                                        420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg
                                                                        472
      <210> 87
      <211> 413
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(413)
      \langle 223 \rangle n = A,T,C or G
      <400> 87
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
                                                                         60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                        120
cototttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
                                                                        180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt
                                                                        240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg
                                                                        300
ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa
                                                                        360
acagaaattg ggtngtatat tgaaananng catcattnaa acgttttttt ttt
                                                                        413
      <210> 88
      <211> 448
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(448)
      \langle 223 \rangle n = A,T,C or G
      <400> 88
equagegggt cotototate tagetecage etetegeetg coccactece egegtecege
                                                                         60
gtectageen accatggeeg ggeecetgeg egeecegetg etectgetgg ecatectgge
                                                                        120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtccc qqcaaqccqc cqcqcctqqt
                                                                       180
gggaggccca tggaccccgc gtggaagaag aaggtgtgcg gcgtgcactq qactttqccq
                                                                        240
teggenanta caacaaacce geaacnactt ttacenagen egegetgeag gttgtgeege
                                                                       300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng
                                                                       360
tttaccagaa ccnagccaat tngaacaatt ncccctccat aacagcccct tttaaaaagg
                                                                       420
gaancantcc tqntcttttc caaatttt
                                                                       448
      <210> 89
      <211> 463
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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<222> (1)...(463)
      \langle 223 \rangle n = A,T,C or G
qaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca
                                                                         60
gtagtgattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc
                                                                        120
agaggtctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt
                                                                        180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcatc
                                                                        240
tttnatgttn agacttgcct ctntnaaatt gctfttgtnt tctgcaggta ctatctgtgg
                                                                        300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn
                                                                        360
aattetetee eeatannaaa acceangeee ttggganaat ttgaaaaang gnteettenn
                                                                        420
aattennana antteagntn teatacaaca naaenggane eec
                                                                        463
      <210> 90
      <211> 400
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(400)
      \langle 223 \rangle n = A,T,C or G
      <400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt
                                                                         60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaaat
                                                                        120
tottcaccag toacatotto taggacottt ttggattcag ttagtataag etottccact
                                                                        180
tcctttgtta agacttcatc tggtaaagtc ttaagttttg tagaaaggaa tttaattgct
                                                                        240
cqttctctaa caatgtcctc tccttgaagt atttggctga acaacccacc tnaagtccct
                                                                        300
ttgtgcatcc attttaaata tacttaatag ggcattggtn cactaggtta aattctgcaa
                                                                        360
gagtcatctg tctgcaaaag ttgcgttagt atatctgcca
                                                                        400
      <210> 91 '
      <211> 480
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(480)
      <223> n = A, T, C \text{ or } G
      <400> 91
gageteggat ceaataatet ttgtetgagg geageacaea tatneagtge eatggnaact
                                                                         60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac
                                                                        120
atgeetettt gaetaeegtg tgeeagtget ggtgattete acacacetee nneegetett
                                                                        180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcacccacga
                                                                        240
qacacttqaa aqqtqtaaca aaqcqactct tqcattqctt tttqtccctc cqqcaccaqt
                                                                        300
tgtcaatact aaccegotgg tttgcctcca tcacatttgt gatctgtagc tctggataca
                                                                        360
totoctgaca gtactgaaga acttottott ttgtttcaaa agcaactott ggtgcctgtt
                                                                        420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa
                                                                        480
      <210> 92
      <211> 477
      <212> DNA
```

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<213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(477)
      \langle 223 \rangle n = A,T,C or G
      <400> 92
atacageeca nateecacea egaagatgeg ettgttgaet gagaacetga tgeggteact
                                                                          60
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195 200 His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr 215 Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp 235 240 225 230 Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val 245 250 255 Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg 260 265 Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly 275 280 285 Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly 290 295 300 Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp 310 <210> 113 <211> 553 <212> PRT <213> Homo sapien <400> 113 Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala 1 5 10 15 Gln Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu 20 25 Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Glu Val Gly Val 35 40 Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly 50 55 Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly 75 Arg Tyr Gly Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile 90 Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu 100 105 Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly 120 Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu 135 140 Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala 145 150 155 Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr 165 170 175 Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu 185 190 Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu 200 205 Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly 215 220 Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His 230 235 Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu 250

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 Ile
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 Cys
 Gly
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 Val
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				100					105					110	Thr		
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	His	Asp			Val	Glu	Gly			Asn	Gln	Leu			Asp	Ile	
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		_				_	_	_			_				_	tgggt gaagt	300 360
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tactgatccc tgatcactgt cctaatgcag gatgtgggaa acagatgagg tcacctctgt
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aantcctqgg t
                                                                          71
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agtaagctgg cccttctaat aaaagaaaat tgaaaggttt ctcactaanc ggaattaant
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ageacanaer coargegggg acanoageca c	ccccgca			210
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ttaagatttg t				131

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50

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gataaacaaa gt
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      <211> 362
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      <220>
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                                                                       360
gg
                                                                       362
      <210> 131
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(332)
      <223> n = A, T, C \text{ or } G
      <400> 131
ctttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccatgca
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gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga
                                                                       120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc
                                                                       180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa
                                                                       240
cttccatctg ttatcactgg agaaagccca gactccccan gacnggtacg gattgtgggc
                                                                       300
atanaaggat tgggtgaagc tggcgttgtg gt
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      <210> 132
      <211> 322
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      \langle 223 \rangle n = A, T, C or G
      <400> 132
actititgcca titigtatat ataaacaatc tigggacatt ciccigaaaa ciaggigicc
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aqtqqctaaq aqaactcqat ttcaagcaat tctgaaagga aaaccagcat gacacaqaat
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ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt
                                                                         180
tttaqcaaqt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttq
                                                                         240
ggatgettet aaaaaaaact ttggtagaga aaataggaat getnaateet agggaageet
                                                                         300
gtaacaatct acaattggtc ca
                                                                         322
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      <211> 278
      <212> DNA
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      <220>
      <221> misc_feature
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      <400> 133
acaagcette acaagtttaa etaaattggg attaatettt etgtanttat etgeataatt
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cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta
                                                                         120
ctatttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg
                                                                         180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt
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cccacgaaac actaataaaa accacagaga ccagcctg
                                                                         278
      <210> 134
      <211> 121
      <212> DNA
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      <220>
      <221> misc_feature
      <222> (1)...(121)
      \langle 223 \rangle n = A,T,C or G
      <400> 134
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tgattctctg aggttaaact tggttttcaa atgttatttt tacttgtatt ttgcttttgg
                                                                         120
                                                                         121
t
      <210> 135
      <211> 350
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(350)
      \langle 223 \rangle n = A,T,C or G
      <400> 135
acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctatacc
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atancaagtg gtgactggtt aagcgtgcga caaaggtcag ctggcacatt acttgtgtgc
                                                                         120
aaacttgata cttttgttct aagtaggaac tagtatacag tncctaggan tggtactcca
                                                                         180
gggtgcccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct
                                                                         240
ccacctcaat caagecetgg gecatgetac etgeaattgg etgaacaaac gtttgetgag
                                                                         300
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt
                                                                         350
```

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<210> 136
      <211> 399
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
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      <223> n = A, T, C \text{ or } G
      <400> 136
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gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct
                                                                         120
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttqqctctqa
                                                                         180
cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag
                                                                         240
aaaactgcag aggcccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtqc
                                                                         300
tcccaqqaac ccgggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg
                                                                         360
ggtgcagang gatgaagcag ccagntgttc tgctgtggt
                                                                         399
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      <211> 165
      <212> DNA
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      <220>
      <221> misc feature
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      \langle 223 \rangle n = A,T,C or G
      <400> 137
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ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga
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ttggctggtc ccactggtgg tcactgtcat tggtggggtt cctgt
                                                                         165
      <210> 138
      <211> 338
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(338)
      \langle 223 \rangle n = A,T,C or G
      <400> 138
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ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa
                                                                         120
tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg
                                                                         180
tcatgtgttt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananqqt
                                                                         240
cangeeteag gaageeteaa gtteeattea getttgeeae tgtacattee eeatntttaa
                                                                         300
aaaaactgat gccttttttt tttttttttg taaaattc
                                                                         338
      <210> 139
      <211> 382
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<212> DNA
      <213> Homo sapien
      <400> 139
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gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga
                                                                         120
attcaaacag acctegtcat teetggtgtg ageetggteg geteacegee tatcatetge
                                                                        180
atttgcctta ctcaggtgct accggactct ggcccctgat gtctgtagtt tcacaggatg
                                                                         240
cottatttgt cttctacacc ccacagggcc ccctacttct teggatgtgt ttttaataat
                                                                         300
gteagetatg tgeeceatee teetteatge ecteecteec ttteetacca etgetgagtg
                                                                         360
gcctggaact tgtttaaagt gt
                                                                         382
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      <211> 200
      <212> DNA
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      <220>
      <221> misc feature
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      \langle 223 \rangle n = A,T,C or G
      <400> 140
accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat
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actiticati taacanciii tgitaagigi caggotgoac tiigotocat anaattatig
                                                                        120
ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt
                                                                        180
atattcagca taaaggagaa
                                                                        200
      <210> 141
      <211> 335
      <212> DNA
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      <220>
      <221> misc_feature
      <222> (1)...(335)
      <223> n = A, T, C \text{ or } G
      <400> 141
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                                                                         60
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt
                                                                        120
atgcatgtag agaacccaaa ctaatttatt aaacaggata gaaacaggct gtctgggtga
                                                                        180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg
                                                                        240
tttttctacc agttcagaga tnggttaatg actanttcca atggggaaaa agcaagatgg
                                                                        300
attcacaaac caagtaattt taaacaaaga cactt
                                                                        335
      <210> 142
      <211> 459
      <212> DNA
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      <220>
      <221> misc_feature
      <222> (1)...(459)
      <223> n = A, T, C \text{ or } G
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<400> 142
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gggttgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat
                                                                        120
ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca
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cacatggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattqqtc
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                                                                        300
teaacacete agtggccace aaaccattea gcacagette ettaactgtg agetgtttga
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agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct
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      <211> 140
      <212> DNA
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aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctqaq
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accatecgae tteectgtgt
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      <211> 164
      <212> DNA
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      <220>
      <221> misc_feature
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      <223> n = A,T,C or G
      <400> 144
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                                                                       120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt
                                                                       164
      <210> 145
      <211> 303
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(303)
      \langle 223 \rangle n = A,T,C or G
acgtagacca tocaactttg tatttgtaat ggcaaacatc cagnagcaat toctaaacaa
                                                                        60
actggagggt atttataccc aattatccca ttcattaaca tgccctcctc ctcaggctat
                                                                       120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca
                                                                       180
gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag
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tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat
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caa
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<210> 146

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<211> 327
      <212> DNA
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      <220>
      <221> misc_feature
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      \langle 223 \rangle n = A,T,C or G
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ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt
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cctgaacagg gagggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc
                                                                        240
agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg
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taggggtgag ctgtgtgact ctatggt
                                                                        327
      <210> 147
      <211> 173
      <212> DNA
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      <220>
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      <223> n = A, T, C \text{ or } G
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                                                                         60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt
                                                                        120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt
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      <210> 148
      <211> 477
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(477)
      <223> n = A, T, C or G
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atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact
                                                                        120
geoctactae etgetgeaat aateacatte cetteetgte etgaceetga agecattqqq
                                                                        180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac
                                                                        240
nccancecae etcacegaee ecateetett acacagetae etcettgete tetaacecea
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tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag
                                                                        360
caccactggt aagcettete cagecaacae acacacaca acacneacae acacacatat
                                                                        420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg
                                                                        477
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      <211> 207
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<212> DNA

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ettetgetet tatgteetea tetgacaaet etttaeeatt titateeteg eteageagga 120 gcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggaag tcatcaacac 180 cotggctagt gagggtgcgg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca 240 gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt 285 <210> 154 <211> 333 <212> DNA <213> Homo sapien <400> 154 accacagtcc tgttgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc 60 accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaaqac 120 cctaagccgg ttacacagct aactcccact ggccctgatt tgtgaaattg ctgctgcctg 180 attggcacag gagtcgaagg tgttcagctc ccctcctccg tggaacgaga ctctqatttq 240 agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg 300 gtcaggcctg tctcatccat atggatcttc cgg 333 <210> 155 <211> 308 <212> DNA <213> Homo sapien <220> <221> misc_feature <222> (1)...(308) $\langle 223 \rangle$ n = A,T,C or G <400> 155 actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg 60 gaaagtgctt tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat 120 ttgaatcacg gtgcatacaa actotootgo otgotootoo tgggcoccaq coccaqcocc 180 atcacagete actgetetgt teatecagge ceageatgta gtggetgatt ettettgget 240 gettttagec tecanaagtt tetetgaage caaccaaace tetangtgta aggeatgetg 300 gccctggt 308 <210> 156 <211> 295 <212> DNA <213> Homo sapien <400> 156 accttgctcg gtgcttggaa catattagga actcaaaata tgagatgata acagtgccta 60 ttattgatta ctgagagaac tgttagacat ttagttgaag attttctaca caggaactga 120 gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctccttgcct cattctatqt 180 ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat 240 aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacaq actat 295 <210> 157 <211> 126 <212> DNA <213> Homo sapien <400> 157 acaagtttaa atagtgctgt cactgtgcat gtgctgaaat qtqaaatcca ccacatttct 60

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natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtggtg
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ccaaccctgt tttcccagtc cacgtagaca gattcacagt geggaattct ggaagetgga
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nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctqcctctq
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tgttcattct ctgatgtcct gt
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      <211> 498
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      <221> misc_feature
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cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn
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      <222> (1)...(380)
      <223> n = A, T, C \text{ or } G
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tgcaatgcat catgctattt catacctaat gagggagttc caggagattc aaccaggaaa

120

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tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt
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      <220>
      <221> misc feature
      <222> (1)...(195)
      \langle 223 \rangle n = A,T,C or G
      <400> 165
acagtttttt atanatatcg acattgccgg cacttgtgtt cagtttcata aagctggtqq
atcogctgtc atcoactatt cottggctag agtaaaaatt attottatag cocatgtccc
                                                                        120
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggq tqccaqqact
                                                                        180
tcctctgaga tgagt
                                                                        195
      <210> 166
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(383)
      \langle 223 \rangle n = A,T,C or G
      <400> 166
acatettagt agtgtggcac atcaggggc catcagggtc acagtcactc atagcetege
                                                                         60
cgaggtegga gtecacacea ceggtgtagg tgtgeteaat ettgggettg gegeeeaeet
                                                                        120
ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt
                                                                        180
tttgcagacc agcctgagca aggggcggat gttcagcttc agctcctcct tcgtcaggtg
                                                                        240
gatgccaacc tegtetangg teegtgggaa getggtgtee aenteaceta caacetqqqe
                                                                        300
gangatetta taaagagget eenagataaa eteeaegaaa ettetetggg agetgetagt
                                                                        360
nggggccttt ttggtgaact ttc
                                                                        383
      <210> 167
      <211> 247
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(247)
      \langle 223 \rangle n = A,T,C or G
      <400> 167
acagagecag acettggeca taaatgaane agagattaag actaaaccee aagteganat
                                                                         60
tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc
                                                                        120
```

```
tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac
                                                                         180
tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tqactctqac
                                                                         240
tgangtc
                                                                         247
      <210> 168
      <211> 273
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(273)
      \langle 223 \rangle n = A,T,C or G
      <400> 168
acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa
                                                                         60
aatccctcan ccttqttctt cacnactqtc tatactqana qtqtcatqtt tccacaaaqq
                                                                         120
gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag tagggtgggc
                                                                         180
aattoccaac ttocttgcca caagetteec aggetttete ceetggaaaa etecagettg
                                                                         24Ô
agtcccagat acactcatgg gctgccctgg gca
                                                                         273
      <210> 169
      <211> 431
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(431)
      \langle 223 \rangle n = A,T,C or G
      <400> 169
acageettgg etteeceaaa eteeacagte teagtgeaga aagateatet teeageagte
                                                                         60
ageteagace agggteaaag gatgtgacat caacagttte tggttteaga acaggtteta
                                                                         120
ctactqtcaa atqaccccc atacttcctc aaaqqctqtq qtaaqttttq cacaqqtqaq
                                                                         180
qqcaqcagaa agggggtant tactgatgga caccatcttc tctqtatact ccacactqac
                                                                         240
cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc
                                                                         300
acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactqq
                                                                         360
aaagtgatet gataetggat tettaattae etteaaaage ttetggggge cateagetge
                                                                         420
tcgaacactg a
                                                                         431
      <210> 170
      <211> 266
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(266)
      \langle 223 \rangle n = A,T,C or G
      <400> 170
acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagttca gaggtggagc
                                                                         60
tcaaggaget etgeaggeat tttgecaane etetecanag canagggage aacetacaet
                                                                         120
ccccgctaga aagacaccag attggagtcc_tgggagggg agttggggtg ggcatttgat
                                                                         180
```

```
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct
                                                                     240
tcaaagctag gggtctggca ggtgga
                                                                     266
     <210> 171
     <211> 1248
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(1248)
     \langle 223 \rangle n = A,T,C or G
     <400> 171
ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca
                                                                      60
ctqqtcatqq aaaacqaatt gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg
                                                                     120
teageequae actqttteca gaagtgagtg cagageteet acaccategg getgggeetg
                                                                     180
cacagtettg aggeegacca agageeaggg ageeagatgg tggaggeeag ceteteegta
                                                                     240
cggcacccag agtacaacag accettgete getaacgace teatgeteat caagttggac
                                                                     300
quatcoqtqt cogagtotga caccatoogg agcatoagca ttgcttcgca gtgccctacc
                                                                     360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc
                                                                     420
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac
                                                                     480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc
                                                                     540
                                                                     600
aacqqtqact ctqqqqqcc cctqatctgc aacgggtact tgcagggcct tgtgtctttc
qqaaaaqccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc
                                                                     660
actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aacccatgaa
                                                                     720
attgacccc aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct
                                                                     780
ceeteaggee caggagteca ggeececage ceetecteee teaaaccaag ggtacagate
                                                                     840
                                                                     900
cocaqceet ectecteaq acceaqqagt coagaceee cageeeetee teecteagac
ccaggagtec agecetect ceeteagace caggagteca gaecececag eccetectee
                                                                     960
ctcaqaccca qqqqtccaqq ccccaaccc ctcctcctc agactcagag gtccaagcc
                                                                    1020
ccaaccente attecceaga eccagaggte caggteccag eccetentee etcagaccea
                                                                    1080
qcqqtccaat qccacctaqa ctntccctgt acacagtgcc cccttgtggc acgttgaccc
                                                                    1140
                                                                    1200
aaccttacca qttqqttttt catttttnqt ccctttcccc taqatccaga aataaagttt
1248
      <210> 172
      <211> 159
      <212> PRT
      <213> Homo sapien
      <220>
      <221> VARIANT
      <222> (1)...(159)
      <223> Xaa = Any Amino Acid
      <400> 172
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
                                   10
                5
1
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
            2.0
                               25
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
                           40
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
                        55
```

<220>

<221> misc_feature <222> (1)...(1459)

```
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
                    70
                                        75
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
                                   90
                85
Cys Ala Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
                               105
                                                    110
           100
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
                                               125
                          120
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
                      135
                                            140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                    150
                                        155
      <210> 173
      <211> 1265
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(1265)
      <223> n = A,T,C \text{ or } G
      <400> 173
ggcagcccgc actcgcagcc ctggcaggcg gcactggtca tggaaaacga attgttctgc
                                                                       60
tegggegtee tggtgeatee geagtgggtg etgteageeg cacactgttt seagaactee
                                                                      120
tacaccatcq gqctqqgcct gcacagtctt gaggccgacc aagagccagg gagccagatg
                                                                      180
gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgct cgctaacgac
                                                                      240
                                                                      300
ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc
                                                                      360
attgettege agtgeectae egeggggaae tettgeeteg titetggetg gggtetgetg
qcqaacqqtq agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg
                                                                      420
cgggggctga cccagagete tgcgteecag gcagaatgee taccgtgctg cagtgegtga
                                                                      480
                                                                      540
acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgacccgctg taccacccca
gcatgttctg.cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg
                                                                      600
ggcccctgat ctgcaacggg tacttgcagg gccttgtgtc tttcggaaaa gccccgtgtg
                                                                      660
gccaagttgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga
                                                                      720
                                                                      780
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac
                                                                      840
atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggag
                                                                      900
tecaggeece cageceetee teceteaaae caagggtaca gateeceage ceeteeteec
tcaqacccaq gagtccagac ccccagccc ctcctccctc agacccagga gtccagccc
                                                                      960
tecteentea gacceaggag tecagaceee ecageeeete eteceteaga eecaggggtt
                                                                     1020
qaqqcccca acccctcctc cttcagaqtc agaggtccaa gcccccaacc cctcgttccc
                                                                     1080
cagacccaga ggtnnaggtc ccagcccctc ttccntcaga cccagnggtc caatgccacc
                                                                     1140
tagattttcc ctgnacacag tgcccccttg tggnangttg acccaacctt accagttggt
                                                                     1200
ttttcatttt tngtcccttt cccctagatc cagaaataaa gtttaagaga ngngcaaaaa
                                                                     1260
                                                                     1265
aaaaa
      <210> 174
      <211> 1459
      <212> DNA
      <213> Homo sapien
```

780

840 900

$\langle 223 \rangle$ n = A,T,C or G

```
<400> 174
qqtcaqccqc acactgtttc cagaagtgag tgcagagctc ctacaccatc gggctqqqcc
                                                                        60
tqcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg
                                                                       120
tacqqcaccc agagtacaac agacccttgc tcgctaacga cctcatgctc atcaaqttqq
                                                                       180
acquatecqt qtccqaqtct gacaccatcc ggagcatcag cattgcttcg caqtqcccta
                                                                       240
ccqcqqqqaa ctcttgcctc gtttctggct ggggtctgct ggcgaacggt gagctcacqq
                                                                       300
gtgtgtgtct geeetettea aggaggteet etgeeeagte gegggggetg acceagaget
                                                                       360
ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tggtgtctga
                                                                       420
ngaggtetge antaagetet atgaceeget gtaccaeece ancatgttet gegeeggegg
                                                                      480
agggcaagac cagaaggact cctgcaacgt gagagaggg aaaggggagg gcaggcgact
                                                                       540
caqqqaaqgq tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag
                                                                       600
atqqaqaqac acacagggag acagtgacaa ctagagagag aaactgagag aaacagagaa
                                                                       660
ataaacacaq qaataaaqaq aaqcaaaqqa aqaqaqaaac aqaaacaqac atqqqqaqqc
                                                                       720
agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tqaqqqcqqt
                                                                       780
qacctccacc caatagaaaa tcctcttata acttttgact ccccaaaaac ctgactaqaa
                                                                      840
atagcetact gttgacgggg agcettacca ataacataaa tagtegattt atgcatacgt
                                                                      900
tttatgcatt catgatatac ctttgttgga attttttgat atttctaagc tacacagttc
                                                                       960
qtctqtqaat ttttttaaat tgttgcaact ctcctaaaat ttttctgatg tgtttattga
                                                                      1020
aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt
                                                                      1080
gtacccagag ggaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa
                                                                      1140
aaatcaaqac tctacaaaga ggctgggcag ggtggctcat gcctgtaatc ccagcacttt
                                                                      1200
qqqaqqcqaq gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaaatg
                                                                      1260
gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt
                                                                      1320
aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt
                                                                      1380
gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct
                                                                      1440
caaaaaaaaa aaaaaaaaa
                                                                      1459
      <210> 175
      <211> 1167
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(1167)
      \langle 223 \rangle n = A,T,C or G
      <400> 175
gcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg
                                                                       60
qtqcatccqc aqtqqqtqct qtcagccqca cactgtttcc agaactccta caccatcggg
                                                                       120
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc
                                                                       180
ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgctcatc
                                                                       240
aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag
                                                                      300
tgccctaccg cggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga
                                                                      360
atgcctaccg tgctgcactg cgtgaacgtg tcggtggtgt ctgaggangt ctgcagtaag
                                                                      420
ctctatgacc cgctgtacca ccccagcatg ttctgcgccg gcggagggca agaccagaag
                                                                       480
qaeteetqea acqqtqaete tqqqqqqeee etgatetqea acqqqtaett geagggeett
                                                                       540
qtqtctttcq qaaaaqcccc gtgtggccaa cttggcgtgc caggtgtcta caccaacctc
                                                                       600
tgcaaattca ctgagtggat agagaaaacc gtccagncca gttaactctg gggactggga
                                                                       660
acccatqaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca
                                                                       720
```

geceeteete ceteaggeee aggagteeag geceecagee ceteeteeet caaaccaagg

gtacagatec ccageceete eteceteaga eccaggagte cagaceeece ageceetent

conteaquee caggagteca gecetecte enteagaege aggagtecag acceeccage

cententeeg teagaceag gggtgeag tecaageee caaceceteg tteceag teagaceag eggtecaatg ceacetag ngttgacea acettaceag ttggtttt ataaagtnta agagaagege aaaaaaaa <210> 176 <211> 205 <212> PRT <213> Homo sapien <220> <221> VARIANT <222> (1)(205) <223> Xaa = Any Amino Ace	ac ccagaggtnc an tntccctgta tc attttttgtc	aggtcccagc ccct	cctccc 1020 gtggca 1080						
<400> 176									
Met Glu Asn Glu Leu Phe Cys Se	r Gly Val Leu 10	Val His Pro Gln 15	Trp						
Val Leu Ser Ala Ala His Cys Ph			Leu						
Gly Leu His Ser Leu Glu Ala As	p Gln Glu Pro		Val						
Glu Ala Ser Leu Ser Val Arg Hi			Leu						
Ala Asn Asp Leu Met Leu Ile Ly 65 70	s Leu Asp Glu 75	-	Ser 80						
Asp Thr Ile Arg Ser Ile Ser Il	e Ala Ser Gln	-							
85 Asn Ser Cys Leu Val Ser Gly Tr	= / =		Met						
Pro Thr Val Leu His Cys Val As			Val						
115 12 Cys Ser Lys Leu Tyr Asp Pro Le		125 Ser Met Phe Cys	Ala						
130 135 Gly Gly Gln Asp Gln Lys As	p Ser Cvs Asn	140 Glv Asp Ser Glv	Glv						
145 150	155		160						
Pro Leu Ile Cys Asn Gly Tyr Le 165	u Gln Gly Leu 170	Val Ser Phe Gly 175	•						
Ala Pro Cys Gly Gln Leu Gly Va 180	l Pro Gly Val 185	Tyr Thr Asn Leu 190	Cys						
Lys Phe Thr Glu Trp Ile Glu Ly 195 20		Xaa Ser 205							
<210> 177 <211> 1119 <212> DNA <213> Homo sapien									
gcgcactcgc agccctggca ggcggcactg gtcatggaaa acgaattgtt ctgctcgggc 60									
gteetggtge atcegeagtg ggtgetgtea geegeacaet gttteeagaa eteetacaee 120 ategggetgg geetgeacag tettgaggee gaecaagage cagggageea gatggtggag 180									
gccagcetet cegtaeggea cecagagt									
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct 300									

360

420

480

540

600

660

720

780

840

900

960 1020

1080

1119

<400> 179

```
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gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga gaagctttcc
caaccetgge agggttgtac cattteggea acttecagtg caaggaegte etgetgeate
ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgatc aactagccag
caccataqtt ctccqaagtc agactatcat gattactqtq ttgactgtqc tqtctattqt
actaaccatg cegatgttta ggtgaaatta gegteacttg geeteaacca tettggtate
caqttatect cactgaattg agattteetg etteagtgte agecatteee acataattte
tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc ccctcacaaa
ttcatttctc ctgttgtagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg
qaqqtqaqqq aqaqqqccca tqqttcaatq qqatctqtqc agttqtaaca cattaqqtqc
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaa
      <210> 178
      <211> 164
      <212> PRT
      <213> Homo sapien
      <220>
      <221> VARIANT
      <222> (1)...(164)
      <223> Xaa = Any Amino Acid
      <400> 178
Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
                5
                                    10
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
                                25
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
                    70
                                        75
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
                                    90
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
                                105
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
                            120
                                                125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
                        135
                                           140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
                    150
                                        155
Pro Gly Thr Leu
      <210> 179
      <211> 250
      <212> DNA
      <213> Homo sapien
```

```
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct
                                                                         60
 ccagetgece eeggeegggg gatgegagge teggageace ettgeeegge tgtgattget
                                                                         120
gccaggcact gttcatctca gcttttctgt ccctttgctc ccggcaagcg cttctgctga
                                                                        180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa
                                                                        240
aaaaaaaaa
                                                                        250
      <210> 180
      <211> 202
      <212> DNA
      <213> Homo sapien
      <400> 180
actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca
                                                                         60
teacceagae ecegeceetg ecegtgeece acgetgetge taacgacagt atgatgetta
                                                                        120
ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc
                                                                        180
tgatttaaaa aaaaaaaaaa aa
                                                                        202
      <210> 181
      <211> 558
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(558)
      \langle 223 \rangle n = A,T,C or G
      <400> 181
tecytttgkt naggtttkkg agacameeck agacetwaan etgtgteaca gaetteyngg
                                                                         60
aatgtttagg cagtgctagt aatttcytcg taatgattct gttattactt tcctnattct
                                                                        120
ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa
                                                                        180
ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca
                                                                        240
aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac
                                                                        300
ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa
                                                                        360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw
                                                                        420
ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt
                                                                        480
aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc
                                                                        540
caaaaaaaa aaaaaaaa
      <210> 182
      <211> 479
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(479)
      \langle 223 \rangle n = A,T,C or G
      <400> 182
acagggwttk grggatgcta agsccccrga rwtygtttga tccaaccctg gcttwttttc
                                                                        60
agaggggaaa atggggccta gaagttacag mscatytagy tggtgcgmtg gcacccctgg
                                                                        120
esteacacag asteecgagt agetgggaet acaggeacac agteactgaa geaggeeetg
                                                                        180
ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca
                                                                        240
ctaaggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca
                                                                        300
```

tactmttcta agtcctcttc cagcctcact ntctcttggc tttctcaata aartctctat awtgstgara aaattaaaat gttctggtty	t ycatctcatg	tttaatttgg	tacgcatara	360 420 4 79
<210> 183 <211> 384 <212> DNA <213> Homo sapien				
<pre><400> 183 aggcgggagc agaagctaaa gccaaagcca agtaccagta ccaataacag tgccagtgca ggtgccagcc tgaccgccac tctcacattt gccagcacca gtggcagctc tggtgcctgt tgttaatcct gccagtcttt ctcttcaagc cagcactcta ggcagccact atcaatcaat gccatttcaa aaaaaaaaaa aaaa</pre>	agtgccagca gggctcttcg ggtttctcct cagggtgcat	ccagtggtgg ctggccttgg acaagtgaga cctcagaaac	cttcagtgct tggagctggt ttttagatat ctactcaaca	60 120 180 240 300 360 384
<210> 184 <211> 496 <212> DNA <213> Homo sapien				
<220> <221> misc_feature <222> (1)(496) <223> n = A,T,C or G				
<pre><400> 184 accgaattgg gaccgctggc ttataagcga agggagatcg agtctatacg ctgaagaaat cccatcctgc teggttctcc ccagatgaca aacgcttcaa ggtgctcatg acccagcaac tgatgtcttt tctgccacct gttacccctc tgagccctga tgcctttttg ccagccatac attatgcttg tgtgaggcaa tcatggtggc tttttctcat attttaaatt actacmagaw taaaaaaaaa aaaaaa</pre>	ttgaccegat aatactetsg egegeeetgt ggagaeteeg tetttggeat atcacceata	gggacaacag acaccgaatc cctctgaggg taaccaaact ccagtctctc aagggaacac	acctgctcag accatcaaga tcccttaaac cttcggactg gtggcgattg atttgacttt	60 120 180 240 300 360 420 480 496
<210> 185 <211> 384 <212> DNA <213> Homo sapien				
<pre><400> 185 gctggtagcc tatggcgkgg cccacggagg caagtatcyt gcgcsgcgtc ttctaccgtc aggaggacat ggacgtggcc ctcatggagc gggcacaccc tcctggggcc caggcgggca tggtgctgct cctcgtcatc ttcctgctcg ttgccatgtt cagttacaca ttcggcaaag gcgcagcgtt accgcctcat ccgg</pre>	cctacctgca acagcaactg cctgcgtctc tggccaacat	gatetteggg ytegteggag ceagtatgee cetgetggte	cagattecce cceggettet aactggetgg aacttgetea	60 120 180 240 300 360 384
<211> 577				

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<212> DNA
      <213> Homo sapien
      <221> misc feature
      <222> (1)...(577)
      <223> n = A,T,C \text{ or } G
      <400> 186
gagttagete etecacaace ttgatgaggt egtetgeagt ggeetetege tteatacege
                                                                         60
threeategic atactgtagg tittgccacca cytectggca tettggggeg qentaatatt
                                                                        120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctggttc tgtcttccgc
                                                                        180
teggtgtgaa aggateteee agaaggagtg etegatette eccacacttt tgatgaettt
                                                                        240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctqaca gtgaggtcac
                                                                        300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttgtgtgg gggkkgaagt
                                                                        360
ctcacccaga ttctgcatta ccagagagcc gtggcaaaag acattgacaa actcgcccag
                                                                        420
gtggaaaaag amcamctcct ggargtgctn gccgctcctc gtcmgttggt ggcagcgctw
                                                                        480
teettttgae acacaaacaa gttaaaggea tttteageee ecagaaantt gteateatee
                                                                        540
aagatntcgc acagcactna tccagttggg attaaat
                                                                        577
      <210> 187
      <211> 534
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(534)
      \langle 223 \rangle n = A,T,C or G
      <400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw
                                                                         60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact
                                                                        120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggta
                                                                        180
tgccctattc acacctgtta aaagggcgct aagcattttt gattcaacat ctttttttt
                                                                        240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc
                                                                        300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag cttygggagc
                                                                        360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg
                                                                        420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctqttctq
                                                                        480
aggatetece agtttattta ceaettgeae aagaaggegt tttetteete agge
                                                                        534
      <210> 188
      <211> 761
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(761)
      <223> n = A, T, C \text{ or } G
      <400> 188
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg
                                                                        60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg
                                                                       120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct
                                                                       180
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<212> DNA

WO 00/04149 PCT/US99/15838 70

ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt 240 tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg 300 qqqqacaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa 360 acaqaaatwr qgtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt 420 gcaaaaaaca tgtacngact tcccgttgag taatgccaag ttgtttttt tatnataaaa 480 cttgcccttc attacatgtt tnaaagtggt gtggtgggcc aaaatattga aatgatggaa 540 ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacaq taatqttgac 600 atgettaatt cacaaatget aattteatta taaatgtttg etaaaataca etttgaacta 660 tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac 720 gaaaataata acattgaaga aaaananaaa aaanaaaaaa a 761 <210> 189 <211> 482 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(482) <223> n = A, T, C or G<400> 189 ttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca 60 caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca 120 aageegeetg etgeettete tgtetgtete etggtgeagg cacatgggga gacetteece 180 aaggcagggg ccaccagtcc aggggtggga atacaggggg tgggangtgt qcataaqaaq 240 tgataggeac aggccaccog gtacagaccc ctcggctcct gacaggtnga tttcqaccaq 300 gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc 360 aaatttggct ngtcatngaa ngggcanttt tccaanttng gctnggtctt ggtacncttg 420 gtteggeeca geteenegte caaaaantat teaccennet eenaattget tgenggneec 480 482 <210> 190 <211> 471 <212> DNA <213> Homo sapien <220> <221> misc feature <222> (1)...(471) $\langle 223 \rangle$ n = A,T,C or G <400> 190 ttttttttt ttttaaaaca gttttcaca acaaaattta ttagaagaat agtggttttg 60 aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtnctcca 120 aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag 180 cgcttttgac atacaatgca caaaaaaaaa agggggggg gaccacatqq attaaaattt 240 taagtactca tcacatacat taagacacag ttctagtcca qtcnaaaatc aqaactqcnt 300 tgaaaaattt catgtatgca atccaaccaa agaacttnat tggtgatcat gantnctcta 360 ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacnengt acaaaaanaa 420 tctgtaattn anttcaacct ccgtacngaa aaatnttnnt tatacactcc c 471 <210> 191 <211> 402

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<213> Homo sapien
       <220>
       <221> misc_feature
       <222> (1)...(402)
       <223> n = A, T, C or G
       <400> 191
gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct
                                                                         60
gtetteeact caetgtetgt aagettttta acceagaewg tatetteata aatagaacaa
                                                                        120
attetteace agteacatet tetaggacet ttttggatte agttagtata agetetteca
                                                                        180
cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg
                                                                        240
ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc
                                                                        300
ctttgtgcat ccattttaaa tatacttaat agggcattgk tncactaggt taaattctgc
                                                                        360
aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca
                                                                        402
      <210> 192
      <211> 601
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(601)
      \langle 223 \rangle n = A,T,C or G
      <400> 192
gageteggat ecaataatet ttgtetgagg geageacaea tatneagtge eatggnaact
                                                                         60
ggtctacccc acatgggage agcatgccgt agntatataa ggtcattccc tqaqtcagac
                                                                        120
atgcytyttt gaytaccgtg tgccaagtgc tggtgattct yaacacacyt ccatcccgyt
                                                                        180
cttttgtgga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc
                                                                        240
acgagacact tgaaaggtgt aacaaagcga ytcttgcatt gctttttgtc cctccggcac
                                                                        300
cagttgtcaa tactaacccg ctggtttgcc tccatcacat ttgtgatctg tagctctgga
                                                                        360
tacatetect gacagtactg aagaacttet tettttgttt caaaagcare tettggtgee
                                                                        420
tgttggatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac
                                                                        480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag
                                                                        540
cetegatgta geeggeeage geeaaggeag gegeegtgag ceecaccage ageagaagea
                                                                        600
                                                                        601
      <210> 193
      <211> 608
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(608)
      <223> n = A, T, C \text{ or } G
      <400> 193
atacagecca nateccaeca egaagatgeg ettgttgaet gagaacetga tgeggteaet
                                                                        60
ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt
                                                                       120
cccaacgcag gcagmagcgg gsccggtcaa tgaactccay tcgtggcttg gggtkgacgg
                                                                       180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac
                                                                       240
ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc
                                                                       300
```

```
agaaccttcc gcctgttctc tggcgtcacc tgcagctgct gccgctgaca ctcqqcctcq
gaccagegga caaacggcrt tgaacageeg caceteaegg atgeceagtg tgtegegete
                                                                        420
caggammgsc accagegtgt ccaggtcaat gteggtgaag cccteegegg gtratggegt
                                                                        480
ctgcagtgtt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcatcgaaga
                                                                        540
gtegegeetg egtgageage atgaaggegt tgteggeteg eagttettet teaggaacte
                                                                        600
cacqcaat
                                                                        608
      <210> 194
      <211> 392
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(392)
      <223> n = A, T, C \text{ or } G
      <400> 194
gaacggctgg accttgcctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt
                                                                        60
ccagtccgag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc
                                                                        120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg
                                                                        180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac
                                                                        240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt
                                                                       300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg
                                                                       360
aaataaatat agttattaaa ggttgtcant cc
                                                                       392
      <210> 195
      <211> 502
      <212> DNA
      <213 > Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(502)
      <223> n = A, T, C \text{ or } G
      <400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg
                                                                        60
ccgagctgag gcagatgttc ccacagtgac ccccagagcc stgggstata gtytctgacc
                                                                       120
cetencaagg aaagaceaes ttetggggae atgggetgga gggeaggaee tagaggeaee
                                                                       180
aagggaagge cccatteegg ggstgtteec egaggaggaa gggaaggge tetgtgtgee
                                                                       240
ccccasgagg aagaggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca
                                                                       300
caaatgcaag ctcaccaagg tcccctctca gtccccttcc stacaccctg amcggccact
                                                                       360
gsescaeace caeeeagage aegeeaceeg ceatggggar tgtgeteaag gartegengg
                                                                       420
gcarcgtgga catcingtcc cagaaggggg cagaatcicc aatagangga cigarcmsti
                                                                       480
gctnanaaaa aaaaanaaaa aa
                                                                       502
      <210> 196
      <211> 665
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(665)
```

<223> n = A,T,C or G

```
<400> 196
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc
                                                                         60
cetetggaag cettgegeag ageggaettt gtaattgttg gagaataact getgaatttt
                                                                        120
wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga
                                                                        180
actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkatc
                                                                        240
aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt
                                                                        300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact
                                                                        360
tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggtatgt
                                                                        420
watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt
                                                                        480
tottgacaga aatogatott gatgotgtgg aagtagtttg accoacatoo otatgagttt
                                                                        540
ttcttagaat gtataaaggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac
                                                                        600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan
                                                                        660
aaqtq
                                                                        665
      <210> 197
      <211> 492
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(492)
      <223> n = A, T, C \text{ or } G
      <400> 197
ttttnttttt tttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat
                                                                        6.0
atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg
                                                                        120
aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag
                                                                        180
aattatagtc naaccagtaa acnaggaatt tacttttcaa aagattaaat ccaaactgaa
                                                                        240
caaaattcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac
                                                                        300
attetettet gaaetttaga ttttetagaa aaatatgtaa tagtgateag gaagagetet
                                                                        360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc
                                                                        420
catttcactc ccatcacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg
                                                                       480
anchtggctt aa
                                                                       492
      <210> 198
      <211> 478
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(478)
      \langle 223 \rangle n = A,T,C or G
      <400> 198
tttnttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa
                                                                        60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac
                                                                       120
tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgccganc atancacatt
                                                                       180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat
                                                                       240
natatatgtc aatcngattt aagatacaaa acagatccta tggtacatan catcntgtag
                                                                       300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta
                                                                       360
agcattctag tacctctact ccatggttaa gaatcgtaca cttatgttta catatgtnca
                                                                       420
```

```
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa
                                                                        478
      <210> 199
       <211> 482
       <212> DNA
       <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(482)
      \langle 223 \rangle n = A,T,C or G
      <400> 199
agtgacttgt cctccaacaa aaccccttga tcaagtttgt ggcactgaca atcagaccta
                                                                         60
tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca
                                                                        120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga
                                                                        180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta
                                                                        240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga
                                                                        300
aaatttacct ggangaaaag aggctttngg ctggggacca tcccattgaa ccttctctta
                                                                        360
anggacttta agaanaaact accacatgtn tgtngtatcc tggtgccngg ccgtttantg
                                                                        420
aacningach neaccettni ggaatanani ettgachgen teetgaacti geteetetge
                                                                        480
ga
                                                                        482
      <210> 200
      <211> 270
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(270)
      <223> n = A, T, C \text{ or } G
      <400> 200
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc
                                                                        60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc
                                                                       120
aaggetgage tgaegeegea gaggtegtgt caegteecae gaeettgaeg eegtegggga
                                                                       180
cagccggaac agagcccggt gaangcggga ggcctcgggg agcccctcgg gaagggcggc
                                                                       240
ccgagagata cgcaggtgca ggtggccgcc
                                                                       270
      <210> 201
      <211> 419
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(419)
      <223> n = A, T, C or G
      <400> 201
ttttttttt ttttggaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca
                                                                        60
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg
                                                                       120
ttgattggtt tgtctttatg ggggcggggt ggggtagggg aaancgaagc anaantaaca
                                                                       180
tggagtgggt gcaccctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg
                                                                       240
```

```
totgtgaccg toattttctt gacatcaatg ttattagaag toaggatatc ttttagagag
                                                                    300
tccactgtnt ctggagggag attagggttt cttgccaana tccaancaaa atccacntga
                                                                    360
aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtqqcca
                                                                    419
      <210> 202
      <211> 509
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(509)
      <223> n = A, T, C \text{ or } G
      <400> 202
60
tggcacttaa tccattttta tttcaaaatg tctacaaant ttnaatncnc cattatacng
                                                                   120
gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaatnnaa
                                                                   180
tacncncaaa aatcaaaaat atacntntct ttcagcaaac ttnqttacat aaattaaaaa
                                                                   240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atntttnnaa
                                                                   300
ggaactaaaa taaaaaaaaa cactnccgca aaggttaaag ggaacaacaa attcntttta
                                                                   360
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng
                                                                   420
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca
                                                                   480
caatggnaat nccnccncnc tggactagt
                                                                   509
     <210> 203
     <211> 583
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc feature
     <222> (1) ... (583)
     <223> n = A,T,C or G
     <400> 203
tttttttttt tttttttga cccccctctt ataaaaaaca agttaccatt ttattttact
                                                                    60
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac
                                                                   120
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt
                                                                   180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc
                                                                   240
attitititi tecetatice aagteaatti
                                                                   300
gettetetag ceteatitee tagetettat etaetattag taagtggett titteetaaa
                                                                   360
agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc
                                                                   420
tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tccttttatg
                                                                   480
tccattttag tcactaaacg atatcnaaag tgccagaatg caaaaggttt gtgaacattt
                                                                   540
attcaaaagc taatataaga tatttcacat actcatcttt ctg
                                                                   583
     <210> 204
     <211> 589
     <212> DNA
     <213> Homo sapien
     <220>
     <221> misc_feature
     <222> (1)...(589)
```

<223> n = A, T, C or G

<400> 204

```
tttttttttt tttttttttt ttttttnctc ttctttttt ttganaatga ggatcgagtt
                                                                         60
tttcactctc tagatagggc atgaagaaaa ctcatctttc cagctttaaa ataacaatca
                                                                        120
aatotottat gotatatoat attttaagtt aaactaatga gtoactggot tatottotoo
                                                                        180
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat
                                                                        240
tgagaggttt ttcttctcta tttacacata tatttccatg tgaatttgta tcaaaccttt
                                                                        300
attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnaq
                                                                        360
cattacaaaa ctgctcaaat tgtttgttaa gnttatccat tataattagt tnggcaggag
                                                                        420
ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc
                                                                        480
aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat
                                                                        540
ttattnagaa tgaattcaca tgttattatt ccntagccca acacaatgg
                                                                        589
      <210> 205
      <211> 545
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1) ... (545)
      <223> n = A,T,C \text{ or } G
      <400> 205
tttttntttt ttttttcagt aataatcaga acaatattta tttttatatt taaaattcat
                                                                        60
agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata
                                                                       120
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat
                                                                       180
ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt
                                                                       240
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat
                                                                       300
atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct
                                                                       360
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt
                                                                       420
aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg
                                                                       480
aaggattaga tatgtttcct ttgccaatat taaaaaaata ataatgttta ctactagtga
                                                                       540
aaccc
                                                                       545
      <210> 206
      <211> 487
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(487)
      <223> n = A, T, C \text{ or } G
      <400> 206
ttttttttt ttttttagtc aagtttctna tttttattat aattaaagtc ttggtcattt
                                                                        60
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna
                                                                       120
caatttataa atgtaaggtg ccattattga gtanatatat tcctccaaga gtggatgtgt
                                                                       180
cccttctccc accaactaat gaancagcaa cattagttta attttattag tagatnatac
                                                                       240
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag
                                                                       300
ttggtnagaa tgcatcanca atctnacaat caacagcaag atgaagctag gcntgggctt
                                                                       360
teggtgaaaa tagaetgtgt etgtetgaat caaatgatet gaeetateet eggtggeaag
                                                                       420
aactettega accgetteet caaaggenge tgecacattt gtggentetn ttgeacttgt
                                                                       480
```

```
ttcaaaa
                                                                        487
      <210> 207
      <211> 332
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(332)
      <223> n = A, T, C \text{ or } G
      <400> 207
tgaattggct aaaagactgc atttttanaa ctagcaactc ttatttcttt cctttaaaaa
                                                                         60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa qqtcactact
                                                                        120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana
                                                                        180
atctttgcat gcagaggagg taaaaggtat tggattttca cagaggaana acacagcgca
                                                                        240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatqqq tqqqacatqq
                                                                        300
aaaagaaggc agcctaggcc ctggggagcc ca
                                                                        332
      <210> 208
      <211> 524
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(524)
      <223> n = A, T, C \text{ or } G
      <400> 208
agggcgtggt gcggagggcg ttactgtttt gtctcagtaa caataaatac aaaaagactg
                                                                        60
gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat
                                                                        120
tttaaaggac atggagettg teacaatgte acaatgteac agtgtgaagg geacaeteac
                                                                        180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact
                                                                        240
tttggcagaa tacttnttga aacttgcaga tgataactaa gatccaagat atttcccaaa
                                                                        300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaaqtc
                                                                       360
atgageceag acaetgaeat caaactaage ceaettagae teeteaceae cagtetgtee
                                                                       420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa
                                                                        480
aaaccattac ctgatccact teeggtaatg caccacettg gtga
                                                                        524
      <210> 209
      <211> 159
      <212> DNA
      <213> Homo sapien
      <400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg
                                                                        60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca
                                                                       120
caaaggactc tcgacccaaa ctgccccaga ccctctcca
                                                                       159
      <210> 210
      <211> 256
      <212> DNA
      <213> Homo sapien
```

```
<220>
      <221> misc feature
      <222> (1) ... (256)
      \langle 223 \rangle n = A,T,C or G
      <400> 210
actocotggc agacaaaggc agaggagaga gototgttag ttotgtgttg ttgaactgcc
                                                                          60
actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacqta
                                                                         120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat
                                                                         180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca
                                                                         240
ccaggatgct aaatca
                                                                         256
      <210> 211
      <211> 264
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(264)
      \langle 223 \rangle n = A,T,C or G
      <400> 211
acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg
actggaacac atacccacat ctttgttctg agggataatt ttctqataaa qtcttqctqt
                                                                         120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta qttaaqqaqa
                                                                         180
ggggagatac attengaaag aggactgaaa gaaatactca aqtnqqaaaa caqaaaaaqa
                                                                         240
aaaaaaggag caaatgagaa gcct
                                                                         264
      <210> 212
      <211> 328
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(328)
      <223> n = A, T, C \text{ or } G
      <400> 212
acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa
                                                                          60
ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatqc caqccqqcaq
                                                                         120
gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag
                                                                         180
ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta
                                                                         240
cccctacnac tctttactct ctgganaggg ccagtggtgg tagctataag cttggccaca
                                                                         300
ttttttttc ctttattcct ttgtcaga
                                                                         328
      <210> 213
      <211> 250
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
```

```
<222> (1)...(250)
      <223> n = A,T,C or G
      <400> 213
acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt
                                                                         60
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                        120
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt
                                                                        180
ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatatc tctctnacct
                                                                        240
tctcatcggt
                                                                        250
      <210> 214
      <211> 444
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(444)
      <223> n = A, T, C or G
      <400> 214
acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaaq
                                                                         60
gatttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg
                                                                        120
tttatatatg cagcaacaat attcaagcgc gacaacaggt tattgaactt gcccgccagt
                                                                        180
tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac
                                                                        240
ccctacgact ctttactctc tggagagggc cagtggtggt agctataagc ttggccacat
                                                                        300
ttttttttcc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag
                                                                        360
agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt
                                                                        420
actttgctct ccctaatata cctc
                                                                        444
      <210> 215
      <211> 366
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(366)
      <223> n = A, T, C \text{ or } G
      <400> 215
acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccaqtt
                                                                        60
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct
                                                                       120
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaaqaqtt
                                                                       180
ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatatc tctctgacct
                                                                       240
tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa
                                                                       300
tccaagetgt tttetacaet gtaaceaggt ttecaaceaa ggtggaaate teetataett
                                                                       360
ggtgcc
                                                                       366
      <210> 216
      <211> 260
      <212> DNA
      <213> Homo sapien
      <220>
```

```
<221> misc feature
      <222> (1)...(260)
      <223> n = A, T, C \text{ or } G
      <400> 216
ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc
                                                                         60
caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc attttttat
                                                                        120
taataaaaag tnnaaaaggc ctcttctcaa cttttttccc ttnggctgga aaatttaaaa
                                                                        180
atcaaaaatt tootnaagtt ntoaagctat catatatact ntatootgaa aaagcaacat
                                                                        240
aattcttcct tccctccttt
                                                                        260
      <210> 217
      <211> 262
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(262)
      \langle 223 \rangle n = A,T,C or G
      <400> 217
acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta
                                                                         60
tettgeetat aattitetat titaataagg aaatageaaa tiggggtggg gggaatgtag
                                                                        120
ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt
                                                                        180
atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta
                                                                        240
atateettea tgettgtaaa gt
                                                                        262
      <210> 218
      <211> 205
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(205)
      \langle 223 \rangle n = A,T,C or G
      <400> 218
accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca
                                                                         60
cccctatcaa ctcccttttg tagtaaactt ggaaccttgg aaatgaccag gccaagactc
                                                                        120
aggestesse agttstastg acctttgtss ttangtntna ngtssaggt tgstaggaaa
                                                                        180
anaaatcagc agacacaggt gtaaa
                                                                        205
      <210> 219
      <211> 114
      <212> DNA
      <213> Homo sapien
      <400> 219
tactgttttg tctcagtaac aataaataca aaaagactgg ttgtgttccg qccccatcca
                                                                         60
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga
                                                                        114
      <210> 220
      <211> 93
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```
<212> DNA
      <213> Homo sapien
      <400> 220
actagocago acaaaaggca gggtagoctg aattgottto tgototttac atttotttta
                                                                         60
aaataagcat ttagtgctca gtccctactg agt
                                                                         93
      <210> 221
      <211> 167
      <212> DNA
     <213> Homo sapien
      <220>
      <221> misc feature
      <222> (1)...(167)
      <223> n = A, T, C \text{ or } G
      <400> 221
actangtgca ggtgcgcaca aatatttgtc gatattccct tcatcttgga ttccatgagg
                                                                         60
tettttgece ageetgtgge tetactgtag taagtttetg etgatgagga geeagnatge
                                                                        120
cececactae ettecetgae getececana aateacecaa ectetgt
                                                                        167
      <210> 222
      <211> 351
      <212> DNA
      <213> Homo sapien
      <400> 222
agggcgtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc
                                                                         60
gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacaqataa
                                                                        120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa
                                                                        180
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt
                                                                        240
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt
                                                                        300
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t
                                                                        351
      <210> 223
      <211> 383
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(383)
      \langle 223 \rangle n = A,T,C or G
      <400> 223
aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat
                                                                         60
tggtaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga
                                                                        120
ttaaaaatgtc tgtgccaaaa ttttgtattt tatttggaga cttcttatca aaagtaatgc
                                                                        180
tgccaaagga agtctaagga attagtagtg ttcccmtcac ttgtttggag tgtgctattc
                                                                        240
taaaagattt tgatttcctg gaatgacaat tatattttaa ctttggtggg ggaaanagtt
                                                                        300
ataggaccac agticticact totgatacti gtaaattaat ottitattigo actigititig
                                                                        360
accattaagc tatatgttta aaa
                                                                        383
```

<210> 224

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<211> 320
      <212> DNA
      <213> Homo sapien
      <400> 224
cccctgaagg cttcttgtta gaaaatagta cagttacaac caataggaac aacaaaaaga
                                                                     60
aaaagtttgt gacattgtag tagggagtgt gtacccctta ctccccatca aaaaaaaaat
                                                                    120
ggatacatgg ttaaaggata raagggcaat attttatcat atgttctaaa agagaaggaa
                                                                    180
gagaaaatac tactttctcr aaatggaagc ccttaaaggt gctttgatac tgaaggacac
                                                                    240
aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgttgcagt
                                                                    300
tttaractcm gcattgtgac
                                                                    320
      <210> 225
      <211> 1214
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      <213> Homo sapien
      <400> 225
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                                                                     60
ttetgetegg gegteetggt geateegeag tgggtgetgt caqeeqeaca etqtttecaq
                                                                    120
aacteetaca eeateggget gggeetgeac agtettgagg eegaecaaga geeaqqqaqe
                                                                    180
cagatggtgg aggccagcct ctccgtacgg cacccagagt acaacagacc cttqctcqct
                                                                    240
aacgacctca tgctcatcaa gttggacgaa tccgtqtccg aqtctqacac catccgqagc
                                                                    300
atcagcattg cttcgcagtg ccctaccgcg gggaactctt gcctcgtttc tqqctqqqqt
                                                                    360
ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaacgtgtc ggtggtgtct
                                                                    420
gaggaggtct gcagtaagct ctatgacccg ctgtaccacc ccagcatgtt ctgcqccqqc
                                                                    480
ggagggcaag accagaagga ctcctgcaac ggtgactctg qqqqqcccct qatctqcaac
                                                                    540
gggtacttgc agggccttgt gtctttcgga aaagccccgt gtggccaagt tggcqtqcca
                                                                    600
ggtgtctaca ccaacctctg caaattcact gagtggatag agaaaaccgt ccaqqccaqt
                                                                    660
taactctggg gactgggaac ccatgaaatt gacccccaaa tacatcctgc ggaaggaatt
                                                                    720
caggaatate tgtteccage ceetecteee teaggeccag gagtecagge ceeeaqeeee
                                                                    780
tectecetea aaccaagggt acagateece agceceteet eecteagace caggagteea
                                                                    840
gacceccag ecectectee etcagaceca ggagtecage ecetectece teagacecag
                                                                    900
gagtccagac cccccagccc ctcctccctc agacccaggg gtccaggccc ccaaccctc
                                                                    960
ctccctcaga ctcagaggtc caagccccca acccctcctt ccccagaccc agaggtccag
                                                                   1020
gteccagece etectecete agacecageg gtecaatgee acetagaete tecetgtaca
                                                                   1080
cagtgccccc ttgtggcacg ttgacccaac cttaccagtt ggtttttcat tttttgtccc
                                                                   1140
1200
aaaaaaaaa aaaa
                                                                   1214
     <210> 226
     <211> 119
     <212> DNA
     <213> Homo sapien
     <400> 226
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                                                                     60
agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacq ataaccagt
                                                                    119
     <210> 227
     <211> 818
     <212> DNA
     <213> Homo sapien
     <400> 227
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					ttctgagaac	120
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					gacaaggcta	240
					tgaaaacgaa	300
					actggaaaag	360
					accatctaga	420
	caccctcagc					480
	tgtcttggga					540
	ggacatgaag					600
	gccctcaagc					660
	ccacaaatcc					720
caagaggata	tgaggactgt	ctcagcctgg	ctttgggctg	acaccatgca	cacacacaag	780
gtccacttct	aggttttcag	cctagatggg	agtcgtgt			818
-210	> 228					
	> 220 > 744					
	> /44 > DNA					
		n				
<213	> Homo sapi	±11				
<400	> 228					
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	ttgacatacc					120
	cctggcctct					180
	ggcttcgtaa					240
	acattggggt					300
	aggccagttt					360
	gaatggcttg					420
	ggatgcttgt					480
	ttggccactc					540
	ccttggccca					600
	taatgttcct					660
	tggaccagag					720
	aagtagctgg		J J	- 55 - 5 5		744
	> 229	4				
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	> DNA					
<213	> Homo sapie	en				
~400·	> 229					
		aaaattaat	aactaattt	atantaanna	+ as+ a+	60
	ttttgtctat					60
	cgaaataaaa					120
ttatatata	ttgtttttta	tactactactg	ttagaaacgt	cacccacagt	ccctgttaat	180
	cagccaactc					240
cactaggete	ctccttgccc	teacaetgga	gtctccgcca	gtgtgggtgc	ccactgacat	300
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	> 301					
	> DNA					
	Homo sapie	en				
<400						
	aatacaaata					60
gagcgacagt	tcaaggagga	gaagcttgca	gagcagctca	agcaagctga	ggagctcagg	120

caatataaag tcctggttca cgggaaggga gagatgcctc gatgaaccgg acaagtccca g	cctctcattg	aatgagcatc	tccaggccct	cctcactccg	180 240 300 301
<210> 231 <211> 301 <212> DNA <213> Homo sapie	en				
<400> 231 gcaagcacgc tggcaaatct caggaactcc aagtccacat ggcaacacgg gacttctcat tctgaggatg gcaggatcaa tttttttgtg gacatgccat c	ccttggcaac caggaagtgg tgatgtcagg	tggggacttg gatgtagatg ccggttggta	cgcaggttag agctgatcaa ccgccaatga	ccttgaggat gacggccagg tgaacacatt	60 120 180 240 300 301
<210> 232 <211> 301 <212> DNA <213> Homo sapie	en				
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<210> 233 <211> 301 <212> DNA <213> Homo sapie	en				
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atgttatett tgaactgatg etcataggag agaatataag aactetgagt gatateaaca
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tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcggcatga tgaccaqcqt 180 gctggtttgt ccagatggca agacagtaga agcagaggct gcccacggga ctgtaacccg 240 teactacege atgttecaga aaggacagga gacgtecace aatcccattg ettecattt 300 301 <210> 244 <211> 300 <212> DNA <213> Homo sapien <400> 244 gctggtttgc aagaatgaaa tgaatgattc tacagctagg acttaacctt gaaatggaaa 60 gtcatgcaat cccatttgca ggatctgtct gtgcacatgc ctctgtagag agcagcattc 120 ccagggacct tggaaacagt tgacactgta aggtgcttgc tccccaagac acatcctaaa 180 aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc ccttcttatt tatgtgaaca 240 actgtttgtc ttttgtgtat cttttttaaa ctgtaaagtt caattgtgaa aatgaatatc 300 <210> 245 <211> 301 <212> DNA <213> Homo sapien <400> 245 gtctgagtat ttaaaatgtt attgaaatta tccccaacca atgttagaaa agaaagaggt 60 tatatactta gataaaaaat gaggtgaatt actatccatt gaaatcatgc tcttagaatt 120 aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata qcagcctat 180 gttttcaaag agcagagatg caattaaata ttgtttagca tcaaaaaggc cactcaatac 240 agctaataaa atgaaagacc taatttctaa agcaattctt tataatttac aaagttttaa 300 g 301 <210> 246 <211> 301 <212> DNA <213> Homo sapien <400> 246 ggtctgtcct acaatgcctg cttcttgaaa gaagtcggca ctttctagaa tagctaaata 60 acctgggctt attttaaaga actatttgta gctcagattg gttttcctat ggctaaaata 120 agtgcttctt gtgaaaatta aataaaacag ttaattcaaa gccttgatat atgttaccac 180 taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc 240 caaatgtgtc ttacaaaaca cgttcctaac aaggtatgct ttacactacc aatgcagaaa 300 301 <210> 247 <211> 301 <212> DNA <213> Homo sapien <400> 247 aggteetttg geagggetea tggateagag eteaaactgg agggaaagge atttegggta 60 gcctaagagg gcgactggcg gcagcacaac caaggaaggc aaggttgttt cccccacqct 120 gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaa caggatcacc catgcgctgc 180 ccttgatgat caaggttggg gcttaagtgg attaagggag gcaagttctg ggttccttgc 240 cttttcaaac catgaagtca ggctctgtat ccctcctttt cctaactgat attctaacta 300 301

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qtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag
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categtaatg aattattttg aaaattaatt eeaccateet tteagattet ggatggaaag
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cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac
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ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta
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ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct
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cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccggaa
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acceccaaaa geetggacac ettgageaca cagttatgac caggacagac teatetetat
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aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt
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t
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tottacctag tocagtotac cocctggagt tagaatggcc atcotgaagt gaaaagtaat
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gtcacattac tcccttcagt gatttcttgt agaagtgcca atccctgaat gccaccaaga
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cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg
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atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtqqtqtcat
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tccagctcac atctcatctg	catgcagcac	ggaccggatg	cgcccactgg	gtcttggctt	240
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C				3 3 5	301
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tagggcaaaa taaataagtg					240
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С					301
2.2					
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ggtgacatcc aatttcttct					240
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С					301
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gagettgetg gtgeagtgea tattggataa cactatteat ggeegaattg ateaagteaa
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                                                                       120
tocaataatt cootcatgat gagcaagaaa aattotttgo gcaccootco tgcatccaca
                                                                       180
gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc
                                                                       240
ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaagcag
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agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa
                                                                       120
gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc
                                                                       180
ttytttctgt ccagagagag tatcagtgac ananatttma gggtgaamac atgmattggt
                                                                       240
gggactinty titacngagm accetgeecg sgegeecteg makengantt eegesanane
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                                                                       301
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      <211> 301
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      <221> misc_feature
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      <400> 274
cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg
                                                                       60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa
                                                                      120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttgtg gaaaagtcca
                                                                      180
totaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc
                                                                      240
aattgtgctt cttttgataa gaagctttct tggtcatatc aggaaattcc aganaaagtc
                                                                      300
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С
                                                                         301
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       <212> DNA
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      <222> (1)...(301)
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gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc
                                                                         120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag
                                                                         180
tcaagagact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc
                                                                         240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat
                                                                         300
                                                                         301
      <210> 276
      <211> 301
      <212> DNA
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                                                                        120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc
                                                                        180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt
                                                                        240
aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat
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                                                                        301
      <210> 277
      <211> 301
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atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg
                                                                        120
gaatcatggc actootgata otttoccaaa tcaacactot caatgcccca cootcgtoot
                                                                        180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga
                                                                        240
gttenetgte gattacatet gaccagtete ettttteega agteenteeg tteaatettg
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C
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      <211> 301
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<220>
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aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca
                                                                        120
cagtetetae tgttattatg cattacetgg gaatttatat aageeettaa taataatgee
                                                                        180
aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgct tcacaqqttt
                                                                        240
tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt
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                                                                        301
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      <211> 301
      <212> DNA
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      <221> misc feature
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gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaaqc
                                                                        120
ttagacettt acetteeage caccecacag tgettgatat tteagagtea gteattggtt
                                                                        180
atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac
                                                                        240
catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacaq
                                                                        300
                                                                        301
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      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 280
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tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct
                                                                       120
tgagaaaaaa acctaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg
                                                                       180
gtttgatata gtttagggtt ggggttagat taagatctaa attacatcag gacaaagaga
                                                                       240
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag
                                                                       300
t
                                                                       301
      <210> 281
      <211> 301
      <212> DNA
      <213> Homo sapien
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gccgagcaat ccaaatcctg aatgaagggg catcttctga aaaaggagat ctgaatctca
                                                                       120
atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt tggagagaaa
                                                                       180
tgtgtagcac actgcgatta cagctaaata acccgtattt gtgtgtcatg tttgcatttc
                                                                       240
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tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc	300 301				
<210> 282 <211> 301 <212> DNA <213> Homo sapien					
<pre><400> 282 caggtactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga agcgcagaag caaagcccag gcagaaccat gctaacctta cagctcagcc tgcacagaag cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg cagaagcaaa gcccaggcag aacatgctaa ccttacagct cagcctgcac agaagcacag a</pre> <pre><210> 283</pre>	60 120 180 240 300 301				
<211> 301 <212> DNA <213> Homo sapien					
<pre><400> 283 atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat tttttctatc acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcatcttta ggaaacatat acattttaa aaatctattt tatgtaagaa ctgacagacg aatttgctt g</pre>	60 120 180 240 300 301				
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caqqaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg
                                                                        180
attaaatatg totgacttot tttgaggtoa cacgactagg caaatgotat ttacgatotg
                                                                        240
caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag
                                                                        300
                                                                        301
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      <211> 301
      <212> DNA
      <213> Homo sapien
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tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagattttt
                                                                        120
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccaccca
                                                                        180
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt
                                                                        240
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg
                                                                        300
                                                                        301
      <210> 287
      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 287
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                                                                         60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg
                                                                        120
anatgatttg gttatgaacg cacagtttag gcagcagggc cagaatcctq accetetgc
                                                                        180
cogtggttat ctcctcccca gcttggctgc ctcatgttat cacagtattc cattttgttt
                                                                        240
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatqc
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                                                                        301
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      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 288
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agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa
                                                                       120
gatctttaaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac
                                                                       180
aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag
                                                                       240
tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaaa
                                                                       300
а
                                                                       301
      <210> 289
      <211> 301
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(301)
      \langle 223 \rangle n = A,T,C or G
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 gettttgatg tetecaagta gtecaeette atttaaetet ttgaaaetgt ateatetttg
                                                                         120
 ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa
                                                                         180
 cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga
                                                                         240
 tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagngga
                                                                         300
                                                                         301
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       <211> 301
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       <223> n = A, T, C or G
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tgactgatct gttcatttct ctcacagctc ttacccccaa aagcttttcc accctaagtg
                                                                        120
ttctgacctc cttttctaat cacagtaggg atagaggcag anccacctac aatgaacatg
                                                                        180
gagttetate aagaggeaga aacageaeag aateeeagtt ttaceatteg etageagtge
                                                                        240
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgaq
                                                                        300
                                                                        301
       <210> 291
       <211> 301
      <212> DNA
      <213> Homo sapien
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caggtaccaa tttcttctat cctagaaaca tttcatttta tgttgttgaa acataacaac
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tatatcagct agattttttt tctatgcttt acctgctatg gaaaatttga cacattctgc
                                                                       120
tttactcttt tgtttatagg tgaatcacaa aatgtatttt tatgtattct gtagttcaat
                                                                       180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa
                                                                       240
acatgagett caetteecca ctaactaatt ageatetgtt atttettaac egtaatgeet
                                                                       300
а
                                                                       301
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      <211> 301
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      <223> n = A, T, C \text{ or } G
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                                                                        60
tgtattaaat aatttttaag tttaaaagat aaaataccat cattttaaat gttggtattc
                                                                       120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg
                                                                       180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc
                                                                       240
tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa
                                                                       300
                                                                       301
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<210> 293
       <211> 301
       <212> DNA
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                                                                         60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt
                                                                        120
aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt
                                                                        180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcatttttaa tgtacctcgg
                                                                        240
cogogaccac gotaagooga attotgoaga tatocatcac actggcggcc gotogagoat
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                                                                        301
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      <211> 301
      <212> DNA
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      <223> n = A, T, C \text{ or } G
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attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag
                                                                       120
tttaactata gtcacaganc ttaaatattc acattgtttt ctatgtctac tgaaaataag
                                                                       180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc
                                                                       240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt
                                                                       300
t
                                                                       3.01
      <210> 295
      <211> 305
      <212> DNA
      <213> Homo sapien
      <400> 295
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cacatttcac tgtgatgtat attgtgttgc aaaaaaaaa gtgtctttgt ttaaaattac
                                                                       120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga
                                                                       180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggt
                                                                       240
tctcagaacc atttcaccca gacagcctgt ttctatcctg tttaataaat tagtttgggt
                                                                       300
tctct
                                                                       305
      <210> 296
      <211> 301
      <212> DNA
      <213> Homo sapien
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                                                                        60
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg
                                                                       120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac
                                                                       180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt
                                                                       240
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tgtcattact ataaatttta aaatctgtt	a ataagatggc	ctatagggag	gaaaaagggg	300 301
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<210> 299 <211> 301 <212> DNA <213> Homo sapien				
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<210> 300 <211> 301 <212> DNA <213> Homo sapien				

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                                                                       120
gctgcattcc acaaggttct cagcctaatg agtttcacta cctgccagtc tcaaaactta
                                                                       180
gtaaagcaag accatgacat tcccccacgg aaatcagagt ttgccccacc gtcttqttac
                                                                       240
tataaageet geetetaaca gteettgett etteacacea ateeegageg cateecceat
                                                                       300
                                                                       301
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      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 301
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agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt
                                                                       120
gggaactcac aaagaccctc agagctgaga cacccacaac agtgggagct cacaaagacc
                                                                       180
ctcagagetg agacacccac aacagtggga getcacaaag accetcagag etgagacace
                                                                       240
cacaacagca cotogttoag otgocacatg tgtgaataag gatgcaatgt ccagaagtgt
                                                                       300
                                                                      301
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      <211> 301
      <212> DNA
      <213> Homo sapien
      <400> 302
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tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac
                                                                      120
ttgagttggt tcttagtatt atttatggta aataggctct taccacttgc aaataactgg
                                                                      180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca
                                                                      240
caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg
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                                                                      301
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      <212> DNA
      <213> Homo sapien
      <400> 303
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atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac
                                                                      120
tggctaatgg aactacegct tgcatgttaa aaatggtggt ttgtgaaatg atcataggcc
                                                                      180
agtaacgggt atgttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc
                                                                      240
categatttt atatetgggg tetagaaaag gagttaatet gtttteeete ataaatteae
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                                                                      301
      <210> 304
      <211> 301
      <212> DNA
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                                                                       60
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tattagtttc agtttcagct tacccacttt ttgtctgcaa catgcaraas agacagtgcc
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 ctttttagtg tatcatatca ggaatcatct cacattggtt tgtgccatta ctggtgcagt
                                                                        180
 gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga
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 ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct
                                                                        300
                                                                        301
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                                                                         60
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggcg
                                                                        120
taaaggagga gaaacagata caaaatctcc aactcagtat taaggtattc tcatgcctag
                                                                        180
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa
                                                                        240
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag
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                                                                       301
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      <400> 306
Val Leu Gly Trp Val Ala Glu Leu
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                                                                       120
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt
                                                                       180
cacaccattg gtgagggagg gattaccacc ctggggttat gaagatggtt gaacacccca
                                                                       240
cacatageae eggagatatg agateaaeag tttettagee atagagatte acageeeaga
                                                                       300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg
                                                                       360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga
                                                                       420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtgaa
                                                                       480
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca
                                                                       540
ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg
                                                                       600
ttacagatac tggggcagca aataaaactg aatcttg
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      <211> 647
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tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa
                                                                        120
ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctq
                                                                        180
ccacccctct gaccctttgg aactcctctg accctttaga acaagcctac ctaatatctg
                                                                        240
ctagagaaaa gaccaacaac ggcctcaaag gatctcttac catgaaggtc tcagctaatt
                                                                        300
cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaaggg tcaatttgct
                                                                        360
cattttgtgt gtggataaag tcaggatgcc caggggccag agcagggggc tgcttgcttt
                                                                        420
gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac
                                                                        480
tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca
                                                                        540
ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc
                                                                       600
aatgteettt ttttteteet gettetgaet tgataaaagg ggaeegt
                                                                        647
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      <211> 460
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      <213> Homo sapien
      <400> 309
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aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg
                                                                       120
gagcacatet teagcaagag ggggaaatae teateatett tggeeageag ttgtttgate
                                                                       180
accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtccg
                                                                       240
ggggaattta ttcctggcaa ttttaattgg actccttatg tgagagcagc ggctacccag
                                                                       300
ctggggtggt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc
                                                                       360
acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat
                                                                       420
ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt
                                                                       460
      <210> 310
      <211> 539
      <212> DNA
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                                                                        60
ctaaaggttt taaaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt
                                                                       120
taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa
                                                                       180
gtcagacagt aagatttgtg ggaaatgggt tggtttgttg tatggtatgt attttagcaa
                                                                       240
taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgctgaa
                                                                       300
ttcctcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac
                                                                       360
ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac
                                                                       420
atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc
                                                                       480
atattttcac ccccacaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga
                                                                       539
      <210> 311
      <211> 526
      <212> DNA
      <213> Homo sapien
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catttacagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa
                                                                       180
attaaacatg gaataaagat tigiccitaa atataatcta caagaagaci tigatatiig
                                                                       240
tttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa
                                                                       300
aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc
                                                                       360
tototttaca gggagotoot gcagococta cagaaatgag tggctgagat tottgattgo
                                                                       420
acagcaagag cttctcatct aaaccctttc cctttttagt atctgtgtat caagtataaa
                                                                       480
agttctataa actgtagtnt acttatttta atccccaaag cacagt
                                                                       526
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      <211> 500
      <212> DNA
      <213> Homo sapien
      <220>
      <221> misc_feature
      <222> (1)...(500)
      <223> n = A, T, C or G
      <400> 312
cottototo cocaccocct qactotagaq aactqqqttt totoccaqta ctocaqcaat
                                                                        60
tcatttctqa aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct
                                                                       120
ccatttetet ttecetteea cetgecagtt ttgetgaete teaacttgte atgagtgtaa
                                                                       180
qcattaagga cattatgett cttcgattet gaagacagge cetgeteatg gatgactetg
                                                                       240
gettettagg aaaatatttt tetteeaaaa teagtaggaa atetaaaett ateeeetett
                                                                       300
tgcagatgtc tagcagcttc agacatttgg ttaagaaccc atgggaaaaa aaaaaatcct
                                                                       360
tgctaatgtg gtttcctttg taaaccanga ttcttatttg nctggtatag aatatcagct
                                                                       420
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt
                                                                       480
tagtcttaat tatctattgg
                                                                       500
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      <213> Homo sapien
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      <221> misc feature
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      \langle 223 \rangle n = A,T,C or G
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tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat
                                                                       120
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa
                                                                       180
gtagtgacat gtttttgcac atttccagcc cttttaaata tccacacaca caggaagcac
                                                                       240
aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga
                                                                       300
gcctcgccct gtgcctgntc ccgcttgtga gggaaggaca ttagaaaatg aattgatgtg
                                                                       360
ttccttaaag gatggcagga aaacagatcc tgttgtggat atttatttga acgggattac
                                                                       420
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agatttgaaa tgaagtcaca aagtgagcat cttgatggtt cacaagacat gcaacaaaca aactggggag gagataccac ggggcagagg cgttatacca atcatttcta tttctaccct ttcttntggc ccacattttc atnatccacc	aaatggaata tcaggattet caaacaaget	ctgtgatgac ggccctgctg gtngaatatc	acgagcagcc cctaactgtg tgacttacgg	480 540 600 660 718
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<211> 151 <212> DNA <213> Homo sapien <400> 316				
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<211> 151 <212> DNA <213> Homo sapien				
<pre><400> 317 agaactagtg gatcctaatg aaatacctga atcttcattt atctctggcc ttaaccctgg ccagggctct gttcttgcca cacctgcttg</pre>	ctcctgaggc			60 120 151
<210> 318 <211> 151 <212> DNA				

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       <222> (1)...(151)
       <223> n = A, T, C or G
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                                                                         60
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                                                                        120
gttcaatyaa aaagacactt ancccatgtg g
                                                                        151
       <210> 324
       <211> 461
       <212> DNA
       <213> Homo sapien
       <220>
      <221> misc_feature
      <222> (1)...(461)
      <223> n = A,T,C \text{ or } G
      <400> 324
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                                                                         60
agaagtggtc agctaaagga atccaggttg ttggttggac tgttaatacc tttgatgaaa
                                                                        120
agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact
                                                                        180
gcgaacctca cttctagact ttcacggtgg gacgaaacgg gttcagaaac tgccaggggc
                                                                        240
ctcatacagg gatatcaaaa taccetttgt getacccagg ccctggggaa tcaggtgact
                                                                        300
cacacaaatg caatagttgg tcactgcatt tttacctgaa ccaaagctaa acccggtgtt
                                                                        360
gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga
                                                                        420
aaaaacgcac aagagcccct gccctgccct agctgangca c
                                                                        461
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      <211> 400
      <212> DNA
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tttgatgtct ccaagtagtc caccttcatt taactctttg aaactgtatc atctttgcca
                                                                        120
agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt
                                                                       180
totataaatg aatgtgotga agcaaagtgo coatggtggo ggogaagaag agaaagatgt
                                                                       240
gttttgtttt ggactctctg tggtcccttc caatgctgtg ggtttccaac caggggaagg
                                                                       300
gtecettttg cattgecaag tgecataace atgageacta egetaceatg gttetgeete
                                                                       360
ctggccaagc aggctggttt gcaagaatga aatgaatgat
                                                                       400
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      <211> 1215
      <212> DNA
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gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg tcagccgcac actgtttcca
                                                                       120
gaacteetae accateggge tgggeetgea cagtettgag geegaecaag ageeagggag
                                                                       180
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300

360

420 480

540

600

660

720

780

840

960

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                                                                   1020
ggtcccagcc cctcctcct cagacccagc ggtccaatgc cacctagact ctccctqtac
                                                                   1080
acaqtqcccc cttqtggcac gttgacccaa ccttaccagt tggtttttca ttttttqtcc
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                                                                   1215
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               5
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Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
                              25
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
                          40
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
                       55
                                          60
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
                   70
                                      75
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
                                  90
Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
                             105
Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
                          120
Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
                      135
                                          140
Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
                  150
                                      155
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
               165
                                  170
Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
                              185
           180
Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
                          200
Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
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215

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      <400> 328
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atccgcagtg ggtgctgtca gccacacact gtttccagaa ctcctacacc atcgggctgg
                                                                      180
gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag gcca
                                                                       234
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      <211> 77
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                                    10
Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
            20
                                25
Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
                            40
His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
                       55
Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
                    70
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      <212> DNA
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      <400> 330
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                                                                       60
gctgcagcca
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      <211> 22
      <212> PRT
      <213> Homo sapien
Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
                5
                                 10
Val Ser Gly Ser Cys Ser
           20
      <210> 332
      <211> 2507
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taaatgtgtc	ttccctcgca	catcacctgg	gaaggatcca	cttccataac	ctgcagggcg	600
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			tggtgtccag			1140
			tttactttgc			1200
			ctcatatgac			1260
			agctatagca			1320
			ctcccaacca			1380
			taacaaagac			1440
			agttcaagac			1500
			ctttgtgtgt			1560
			cacaataatc			1620
			caaagggaag			1680
			ggaagaagta			1740
			gttaaggatt			1800
			aaatatgcta			1860
			aacaaaaacc			1920
			aacaaaaaaa			1980
			ggtcaattta			2040
			tgtgccaaaa			2100
			agtctaagga			2160
			tgatttcctg			2220
			agtcttcact			2280
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_	J	5 5				
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	-					
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tataaagaat ttttttttt c
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                                                                      120
cagaagggte tgaactetae gtgttaceag agaacataat gcaatteatg cattecaett
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		tcatggtgtc				720
		aaatgcatgt				780
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		cctaccaatg				240
		tcataccaac				300
		gtaaggctca				360
		aagctgttca				420
		ggatttcttc				480
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		cagatataaa				300
		ggaagcaaca				360
		ataatatgta				420
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cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920
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gttatgaaga tggttgaaca ccccacacat agcaccggag atatgagatc aacagtttct 2880
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acaagacggt ggggcaaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060
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<210> 383
<211> 155
<212> PRT
<213> Homo sapiens
<400> 383
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Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
                                 25
His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
                             40
Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
                 85
                                     90
Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
                                105
Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
                            120
Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
                        135
Ala Leu Glu Arg Gly His Leu Val Arg Glu
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<210> 384
<211> 557
<212> DNA
<213> Homo sapiens
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ggggaagggt cocttttgca ttgccaagtg ccataaccat gagcactact ctaccatggt 180
totgootcot ggccaagcag gotggtttgc aagaatgaaa tgaatgattc tacaqctaqq 240
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatqc 300
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
tececcaagae acateetaaa aggtgttgta atggtgaaaa egtetteett etttattgee 420
ccttcttatt tatgtgaaca actgtttgtc ttttttttgta tcttttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga ttttttttc aaagtaaaaa 540
aaaaaaaaa aaaaaaa
<210> 385
<211> 337
<212> DNA
<213> Homo sapiens
<400> 385
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gtttctctag cagcagatgg gttaggagga agtgacccaa qtqqttqact cctatqtqca 120
totcaaagoo atotgotgto ttogagtacg gacacatcat cactootgca ttgttgatca 180
aaacgtggag gtgcttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300
ctttggccac caattccccc ttttccacat cccggca
                                                                  337
<210> 386
<211> 300
<212> DNA
<213> Homo sapiens
<400> 386
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geoegetegg eccagagggt gggegeggg etgeetetac eggetggegg etgtaactea 120
gcgaccttgg cccgaaggct ctagcaagga cccaccgacc ccagccgcgg cggcggcggc 180
gcggactttg cccggtgtgt ggggcggagc ggactgcgtg tccgcggacg ggcagcgaag 240
atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300
<210> 387
<211> 537
<212> DNA
<213> Homo sapiens
<400> 387
gggccgagtc gggcaccaag ggactctttg caggcttcct tcctcggatc atcaaggctg 60
ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga ccggcttctg ggcggctgaa agggcaagg aggcaaggac cccgtctctc 180
ccacggatgg ggagaggca ggaggagacc cagccaagtg ccttttcctc aqcactqaqq 240
gagggggett gtttcccttc cctcccggcg acaagctcca gggcagggct gtccctctgg 300
```

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geggeecage acttecteag acacaactte tteetgetge tecagtegtg gggateatea 360
cttacccacc ccccaagttc aagaccaaat cttccagctg cccccttcgt gtttccctgt 420
qtttqctqta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg tgtaqtctcc 480
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<210> 388
<211> 520
<212> DNA
<213> Homo sapiens
<400> 388
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gtttgaagat tgcctcttct acagcttctg agaattgtgt tatttcactt gccaagtgaa 180
ggaccccctc cccaacatgc cccagcccac ccctaagcat ggtcccttgt caccagccaa 240
ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300
acttccccca ccccagaaga ttagcatccc atactagact catactcaac tcaactaggc 360
tcatactcaa ttgatggtta ttagacaatt ccatttcttt ctggttatta taaacaqaaa 420
atctttcctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatqatttct 480
atgaacttgt cttattttaa tggtgggttt tttttctggt
<210> 389
<211> 365
<212> DNA
<213> Homo sapiens
<400> 389
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gagttaaggc tggatttcag atctgcctqq ttccaqccqc aqtqtqccct ctqctccccc 120
aacgactttc caaataatct caccagegee ttccagetca ggegteetaq aaqeqtettq 180
aagcctatgg ccagctgtct ttgtgttccc tctcaccege ctgtcctcac agctgagact 240
cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
gggag
<210> 390
<211> 221
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A, T, C \text{ or } G
<400> 390
tgcctctcca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggntt ctcatgggtg tggaacatct ctgcttgcgg tttcaggaag gcctctggct 120
getetangag tetganenga ntegttgece cantntgaca naaggaaagg eggagettat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a
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<210> 391
<211> 325
<212> DNA
<213> Homo sapiens
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```
<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A,T,C or G
<400> 391
tggagcaggt cocgaggcct coctagagcc tggggccgac tctgtgncga tgcangcttt 60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagecagge actgetgeca acagecagte ennataceat catginacee ggtgngetet 180
naantingat niccanagee clacecaten tagticiget eleccacegg niaceageee 240
cactgcccag gaatcctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300
gagacctccg gctactacta tqacc
                                                                 325
<210> 392
<211> 277
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(277)
\langle 223 \rangle n = A,T,C or G
<400> 392
atattgttta actecttect ttatatettt taacatttte atggngaaag gtteacatet 60
agteteactt nggenagngn etectaettg agtetettee eeggeetgnn eeagtngnaa 120
antaccanga accgncatgn cttaanaacn ncctggtttn tgggttnntc aatgactgca 180
tgcagtgcac caccetgtcc actacgtgat getgtaggat taaagtetca cagtgggegg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa
<210> 393
<211> 566
<212> DNA
<213> Homo sapiens
<400> 393
actagtccag tgtggtggaa ttcgcggccg cgtcgacgga caggtcagct gtctggctca 60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggtct agtttgtcca tcagcattat catgatatca ggactggtta cttggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
cattlattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
cattetetge etgagtttta atttttgtee aaagttattt taatetatae aattaaaage 540
ttttgcctat caaaaaaaa aaaaaa
                                                                566
<210> 394
<211> 384
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
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<222> (1)...(384)
<223> n = A,T,C or G
<400> 394
gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc 60
tgcaaattng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa agggggcagt aattacccaa atccggttgg agcatgacgt 240
gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
tgagcagatg gtttctgagg acgt
<210> 395
<211> 399
<212> DNA
<213> Homo sapiens
<400> 395
ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
tetgacettg gaetecaaga ectacateaa eageetgget atattagatg atgageeagt 120
tatcagaggt ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctqaaqt 180
atteacgtet ttecagtace etgagttere tatagagttg cetaacacag geagaattgg 240
ccagetactt gtetgcaatt gtatetteaa gaataceetg gecateeett tgactgaegt 300
caagttetet ttggaaagee tgggeatete eteactacag acetetgace atgggaeggt 360
gcagcctggt gagaccatcc aatcccaaat aaaatgcac
<210> 396
<211> 403
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(403)
<223> n = A,T,C or G
<400> 396
tggagttntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcataactc tctagagaaa aaaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttagggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
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<210> 397
<211> 100
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(100)
<223> n = A,T,C or G
```

```
<400> 397
actagincag igiggiggaa ticgcggccg cgicgaccia naanccaici ciatagcaaa 60
tecateceeg etectggttg gtnacagaat gactgacaaa
<210> 398
<211> 278
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1) ... (278)
<223> n = A, T, C \text{ or } G
<400> 398
geggeegegt egacageagt teegeeageg etegeeeetg ggtggggatg tgetgeacge 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
teactactgt geetegacea gtgaggagag etggacegae agegaggtgg acteateatq 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg
<210> 399
<211> 298
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(298)
<223> n = A, T, C \text{ or } G
<400> 399
acggaggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120
ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtgqaq cqcatqqqct 180
ceggcattga gegcatggge cegetgggee tegaceacat ggeetecane attganegea 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggq
<210> 400
<211> 548
<212> DNA
<213> Homo sapiens
<400> 400
acatcaacta cttcctcatt ttaaggtatg gcagttccct tcatcccctt ttcctqcctt 60
gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120
tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
tgcagagggc tagagaatta tttcatacag gctttgaggc cacccatgtc acttatcccg 300
tataccetet caccatecee ttgtetacte tgatgeecee aagatgeaac tgggeageta 360
gttggcccca taattctggg cetttgttgt ttgttttaat tacttgggca teecaggaag 420
ctttccagtg atctcctacc atgggccccc ctcctgggat caagcccctc ccaqqccctq 480
tecceageee etectgeece ageceaeeeg ettgeettgg tgeteageee teccattggg 540
agcaggtt
                                                                548
```

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<210> 401
<211> 355
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(355)
\langle 223 \rangle n = A,T,C or G
<400> 401
actqtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaaq 120
taagagtggt ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtgccc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaaqqqt 300
cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatqqn tctqc
<210> 402
<211> 407
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(407)
<223> n = A,T,C or G
<400> 402
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
teteacatge ggtggcatae ataggeteaa aataaaggaa tggagaaaaa tattteaage 120
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttqctqaqq 300
ttgtggaget teteceetge agagagteee tgateteeea aaatttggtt qagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa
<210> 403
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A, T, C or G
<400> 403
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tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tottaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga
                                                                   303
```

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<210> 404
<211> 225
<212> DNA
<213> Homo sapiens
<400> 404
aagtgtaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attqttaatq cactcattta cctttacatq qtgaaaqttc tctcttqatc ctacaaacaq 120
acattttcca ctcqtqtttc cataqttgtt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaaqtqc ctgtgtaata aataaagtat ctttatttca ttcat
<210> 405
<211> 334
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(334)
<223> n = A, T, C \text{ or } G
<400> 405
gagetgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
ttcaatacac ctcccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
teatececat eccatgecaa aggaagaeee teeeteettg geteacagee ttetetagge 180
ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactetecae teteteanng tggateceae cect
<210> 406
<211> 216
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A, T, C \text{ or } G
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant
<210> 407
<211> 413
<212> DNA
<213> Homo sapiens
<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
qtaaatqcaa taqqattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
qtacaacatt gcacccagtg teagatteta cacctggcca etcaggaage aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
```

```
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag
<210> 408
<211> 183
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(183)
\langle 223 \rangle n = A,T,C or G
<400> 408
ggagetngcc ctcaattect ccatnictat gitancatat ttaatgictt tignnattaa 60
tnottaacta gttaatoott aaagggotan ntaatootta actagtooot coattgtqaq 120
cattateett ecagtatten cettetnttt tatttaetee tteetggeta eccatgtaet 180
ntt
<210> 409
<211> 250
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(250)
\langle 223 \rangle n = A,T,C or G
<400> 409
cccacgcatg ataagctett tatttetgta agteetgeta ggaaateate aaatetgaeg 60
gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctqctcacqq ccttatctaq 180
getteecagt geeeceagga eagegtggge tatgtttaea gegenteett getggggggg 240
ggccntatgc
<210> 410
<211> 306
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(306)
\langle 223 \rangle n = A,T,C or G
<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtottgcaa toccatttgc aggatocgto tgtgcacatg cototqtaga gagcagcatt 120
cccagggacc ttggaaacag ttggcactgt aaggtgcttg ctccccaaga cacatcctaa 180
aaggtgttgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atctttttta aactggaaag ttcaattgng aaaatgaata 300
tentge
                                                                    306
```

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<210> 411
<211> 261
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(261)
<223> n = A,T,C or G
<400> 411
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggngaggcaa a
<210> 412
<211> 241
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(241)
<223> n = A, T, C \text{ or } G
<400> 412
gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaaat aattgtgttt cttgcccagg aaatactacq 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggagggag 180
ctgggagatt tcactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
<210> 413
<211> 231
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(231)
\langle 223 \rangle n = A,T,C or G
<400> 413
aactottaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
agaatcettg aatcanttet cagatcattg gggacaccan atcaggaace t
<210> 414
<211> 234
<212> DNA
<213> Homo sapiens
```

```
<400> 414
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagetg aaaacataac ccactetgte etggaggeac tgggaageet agagaagget 120
gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca
<210> 415
<211> 217
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(217)
<223> n = A,T,C or G
<400> 415
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
caaaacacag accaggtage aaatetecac tgetetaagg nteteaceae caetttetea 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc
                                                                    217
<210> 416
<211> 213
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(213)
\langle 223 \rangle n = A,T,C or G
<400> 416
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag
                                                                    213
<210> 417
<211> 303
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(303)
\langle 223 \rangle n = A,T,C or G
<400> 417
nagtetteag geceateagg gaagtteaca etggagagaa gteatacata tgtaetgtat 60
gtgggaaagg ctttactctg agttcaaatc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
teantcaaag ttegtatett caaateeate ngaaggneea cagtatanan aaacetttta 300
                                                                    303
agt
```

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<210> 418
<211> 328
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(328)
\langle 223 \rangle n = A,T,C or G
<400> 418
tttttggcgg tggtggggca gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcactacaac ccctgcctcc catgtccaag cgattcttgt 120
geeteageet teeetgtage tagaattaca ggeacatgee accaeaceea getagttttt 180
gtatttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
teagngqtea ggetggtete aaacteetga eetcaagtga tetgeecace teageeteee 300
aaagtgctan gattacaggc cgtgagcc
<210> 419
<211> 389
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(389)
<223> n = A, T, C or G
<400> 419
cotcotcaaq acqqcotqtg gtccgcctcc cggcaaccaa gaaqcctqca qtqccatatq 60
acccctqage catqqactqq aqcctqaaaq qcaqcqtaca ccctqctcct qatcttqctq 120
cttqtttcct ctctgtggct ccattcatag cacagttgtt gcactgaggc ttgtgcaqqc 180
cqaqcaaqqc caaqctggct caaagagcaa ccagtcaact ctgccacqqt qtqccaqqca 240
cogqttctcc agccaccaac ctcactogct cocgcaaatg gcacatcagt tottctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg
                                                                   389
<210> 420
<211> 408
<212> DNA
<213> Homo sapiens
<400> 420
gtteeteeta aeteetgeea gaaacagete teeteaacat gagagetgea eeeeteetee 60
tggccagggc agcaagcett agcettgget tettgtttet gettttttte tggetagace 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attettgaat gagteetata aacatgaaca ggtttatatt egaageacag 360
acgttgaccg gactttgatg aagtgctatg acaaacctgg caagcccg
<210> 421
<211> 352
<212> DNA
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<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(352)
<223> n = A,T,C or G
<400> 421
gctcaaaaat ctttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct tttttgggtc cttcttctcc accacnatat acttgcagtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaaq 240
ggtgcaacat gaaatttetg tttegtagea agtgcatgte teacaagttg gcangtetge 300
cacteegagt ttattgggtg tttgttteet ttgagateea tgeattteet gg
<210> 422
<211> 337
<212> DNA
<213> Homo sapiens
<400> 422
atgccaccat gctggcaatg cagegggegg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatega eggcaacegt tgcccgaagt tgccgatgcc agccgaageg gtggtcaaqq 120
gegatageaa ggtgeeggeg ategeggegg egteaateet ggeeaaggte ageegtgate 180
gtgaaatggc agctgtcqaa ttqatctacc cqqqttatqq catcqqcqqq cataaqqqct 240
atcogacaco ggtgcacotg gaagcottgc agoggctggg gccgacgccg attcaccqac 300
gcttcttccg ccggtacggc tggcctatga aaattat
                                                                    337
<210> 423
<211> 310
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(310)
\langle 223 \rangle n = A,T,C or G
<400> 423
gctcaaaaat ctttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
teactgacag aacaggtett ttttgggtee ttetteteea ceaegatata ettgeagtee 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaqqtqt anaaacaaqq 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta
                                                                    310
<210> 424
<211> 370
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(370)
\langle 223 \rangle n = A,T,C or G
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<400> 424
gctcaaaaat ctttttactg ataggcatgg ctacacaatc attqactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggicitt titigggicci icticiccac cacgatatac itgcagicci 180
cettettgaa gattetttgg cagttgtett tgtcataacc cacaggtgta gaaacateet 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg
<210> 425
<211> 216
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A, T, C \text{ or } G
<400> 425
taacaacnca acatcaaggn aaananaaca ggaatggntg actntqcata aatnqqccqa 120
anattateea ttatnttaag ggttgaette aggntaeage acacagaeaa acatgeecag 180°
gaggntntca ggaccgctcg atgtnttntq aqqaqq
                                                                216
<210> 426
<211> 596
<212> DNA
<213> Homo sapiens
<400> 426
cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gccccaaggg tcgctggcca 120
getetetgtt ttgetgagtt ggeagtagga eetaatttgt taattaagag tagatggtga 180
getgteettg tattttgatt aacctaatgg cetteecage aegactegga tteagetgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggcca ttaagaggca cttcccgtta 300
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtqqccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atcttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct
<210> 427
<211> 107
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(107)
<223> n = A,T,C or G
<400> 427
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
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ceegggagea geettanaga geteetgttt gaetgeeegg eteagng
                                                                    107
<210> 428
<211> 38
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(38)
<223> n = A, T, C or G
<400> 428
gaacttccna anaangactt tattcactat tttacatt
                                                                   38
<210> 429
<211> 544
<212> DNA
<213> Homo sapiens
<400> 429
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cqctqcattt 60
attgaagage ggetgeagee etgeggttea gattaaaate egagaattgt atagaegeeg 120
atatccacga actettgaag gaetttetga tttatccaca atcaaatcat eggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttccact tcagttacac ctcactcacc atcctctcct gttggttctg tgctqcttca 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgccctttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat
<210> 430
<211> 507
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(507)
\langle 223 \rangle n = A,T,C or G
<400> 430
cttatencaa tggggcteec aaacttgget gtgeagtgga aacteegggg gaattttgaa 60
gaacactgac acceatette cacceegaca etetgattta attgggetge agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttgtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggaq 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
catteteete tggeetetaa tagteaatga ttgtgtagee atgeetatea gtaaaaaqat 480
ttttgagcaa aaaaaaaaa aaaaaaa
                                                                   507
<210> 431
<211> 392
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<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A, T, C \text{ or } G
<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatqttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggcttttac tctgctgttt ct
                                                                    392
<210> 432
<211> 387
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A,T,C or G
<400> 432
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatetettg tettattett ttgtetataa taetgtattg 120
ngtagtccaa gctctcggna gtccagccac tgngaaacat gctcccttta gattaacctc 180
gtggacnetn ttgttgnatt gtetgaactg tagngeeetg tattttgett etgtetgnga 240
attetgttge ttetggggea ttteettgng atgeagagga ceaceaeaa gatgaeagea 300
atotgaattg ntocaatcac agotgogatt aagacatact gaaatogtac aggacoggga 360
acaacgtata gaacactgga gtccttt
                                                                    387
<210> 433
<211> 281
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(281)
<223> n = A, T, C \text{ or } G
<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggenetat ttgggttgge tggaggaget gtggaaaaca tggagagatt ggegetggag 180
ategeogtgg ctatteeten ttgntattae accagngagg ntetetgtnt geccaetggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t
                                                                   281
<210> 434
<211> 484
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<212> DNA
<213> Homo sapiens
<400> 434
ttttaaaata agcatttagt geteagteee taetgagtae tetttetete eeeteetetg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tgttgcaaaa aaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaaccat ttcacccaga 300
cagcetgttt ctateetgtt taataaatta gtttgggtte tetacatgea taacaaacce 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag tacccatgtc 480
ttta
<210> 435
<211> 424
<212> DNA
<213> Homo sapiens
<400> 435
qeqeeqetea qaqeaqqtea etttetgeet tecaegteet eetteaagga ageeceatgt 60
gggtagettt caatategea ggttettaet eetetgeete tataagetea aacceaceaa 120
cqatcqqqca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctqt ggggaggg caagatagat gagggggagc ggcatggtgc ggggtgaccc 240
cttggagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
qqtaqaqacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac
<210> 436
<211> 667
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(667)
<223> n = A, T, C \text{ or } G
<400> 436
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctqqccat gtaatcctqa aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agectettet ggaatteete tgattteaaa gteteaetet caagttettg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggtcaacgt ctgtgcttcg aatataaacc 360
tqttcatqtt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
gatteettta tggggteagt gggaaaggtg teaatgggae tteggtetee atgeegaaac 540
accaaaqtca caaacttcaa ctccttqqct aqtacacttc qqtctaqcca gaaaaaaaqc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag
                                                                   667
<210> 437
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<211> 693

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<212> DNA
<213> Homo sapiens
<400> 437
ctacqtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaact tcagacagct ttttcagatc 180
aggtacteet ctatttteac ceetettget tetactetet ggeagteaga cetgtgggag 300
gccatgggag aaagcagctc tctggatqtt tqtacaqatc atqqactatt ctctqtqqac 360
catttctcca ggttacccta ggtgtcacta ttggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaacttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tectatttet aggeactgag ggetgtgggg tacettgtgg tgecaaaaca gateetgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg qctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc
<210> 438
<211> 360
<212> DNA
<213> Homo sapiens
<400> 438
ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcca aagaatcttc aagaaqqaqq 180
actgcaagta tatctggtgg agaagaagga cccaaaaaaag acctgttctg tcagtgaatq 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctq 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360
<210> 439
<211> 431
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(431)
\langle 223 \rangle n = A,T,C or G
<400> 439
gttcctnnta actcctgcca gaaacagctc tcctcaacat gagagctgca cccttcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tqqctaqacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggaqaccqaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatqqcca caaqqatttq 240
gccaactcac ccagctgggc atggagcagc attatgaact tggaqaqtat ataaqaaaqa 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag t
                                                                431
<210> 440
<211> 523
<212> DNA
<213> Homo sapiens
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<400> 440
agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
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tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta
<210> 441
<211> 430
<212> DNA
<213> Homo sapiens
<400> 441
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagetgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attettgaat gagteetata aacatgaaca ggtttatatt egaageacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag
<210> 442
<211> 362
<212> DNA
<213> Homo sapiens
<400> 442
ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tggtggggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgttttgacc attaagctat 180
atqtttaqaa atqqtcattt tacqqaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc
<210> 443
<211> 624
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(624)
<223> n = A, T, C or G
<400> 443
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgettatt ttaaaagaaa tgtaaagage agaaageaat teaggetace etgeettttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
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cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaaatgaac 360
taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca teettattat taaagteaac getaaaatga atgtgtgtge atatgetaat 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaaggttt cctggaaaga 540
ngatgettqt getgggteea aatettggte taetatgace ttggceaaat tatttaaaet 600
ttgtccctat ctgctaaaca gatc
<210> 444
<211> 425
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1) ... (425)
\langle 223 \rangle n = A,T,C or G
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gaagetttgt ccaggeetgt gtgtgaacce aatgttttge ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg gctgaaagag caaccagcca 300
cetetgeaat etgecacete etgetgeag gatttgtttt tgeateetgt gaagageeaa 360
qqaqqcacca qggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
                                                                    425
gtaga
<210> 445
<211> 414
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(414)
\langle 223 \rangle n = A,T,C or G
<400> 445
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ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattett tgeatgtgge agattattgg atgtagttte etttaactag catataaate 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatqaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggatttttat aatoctacto acaaatgact aggottotoo tottgtattt tgaagcagtg 360.
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcgaattta gtag
<210> 446
<211> 631
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(631)
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\langle 223 \rangle n = A,T,C or G
<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatqqct 60
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atgctggtta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttgttc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaactttc caaccttcca ggaaatgccc cagaaqcaac aqaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttqqa ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg catttgtggt 540
aatctacacc aatgaaaaca tgtactacag ctatatttga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgttttttct g
<210> 447
<211> 585
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(585)
<223> n = A, T, C or G
<400> 447
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cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctq qaattcctct qatttcaaag tctcactctc aagttcttqa aaacqagggc 180
agtteetgaa aggeaggtat ageaactgat etteaqaaaq aggaactgtq tqeaccqqqa 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
atteetttat ggggteagtg ggaaaggtgt caatgggact teggteteea tgeegaaaca 540
ccaaagtcac aaacttcaac tccttggcta gtacacttcg gtcta
<210> 448
<211> 93
<212> DNA
<213> Homo sapiens
<220>
<221> misc feature
<222> (1)...(93)
\langle 223 \rangle n = A,T,C or G
tgctcgtggg tcattctgan nnccgaactg acentgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag
                                                                    93
<210> 449
<211> 706
<212> DNA
<213> Homo sapiens
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<220>
<221> misc_feature
<222> (1)...(706)
<223> n = A,T,C or G
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ttctqancac cqaactgacc atgccaqccc tgccgatggt cctccatggc tccctaqtqc 120
cctqqaqagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
eggggacage atcetgcaga tggtegggeg egteceatte gccatteagg etgegcaaet 240
qttqqqaaqq qcqatcqqtq cqqqcctctt cqctattacq ccaqctqqcq aaaqqqqqat 300
gtgctgcaag gcgattaagt tgggtaacgc cagggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacqtggga tccncactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgaggag aagetggagg cacaacgene cagacactca cagetactca ggaggetgag 600
aacaqqttqa acctqqqaqq tqqaqqttqc aatqaqctqa qatcagqccn ctqcncccca 660
<210> 450
<211> 493
<212> DNA
<213> Homo sapiens
<400> 450
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acaqttttaa aaqqtaaaac aacataaaaa qaaatatcct ataqtqqaaa taaqaqaqtc 120
aaatqaqqct qaqaacttta caaaqqqatc ttacaqacat qtcqccaata tcactqcatq 180
agcctaaqta taaqaacaac ctttqqqqag aaaccatcat ttqacaqtqa qqtacaattc 240
caaqtcagqt aqtqaaatqq gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg toagagagtt aaaaagtgag ttotatocat gaggtgatto cacagtotto 360
tcaaqtcaac acatctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagetttac aaacteecat tgeegagggt egaegeggee 480
gcgaatttag tag
                                                                 493
<210> 451
<211> 501
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(501)
\langle 223 \rangle n = A,T,C or G
<400> 451
gggegegtee cattegeeat teaggetgeg caactgttgg gaagggegat eggtgeggge 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
qeqqeeqect actactacta aattegegge egegtegaeg tgggateene actgagagag 300
tqqaqaqtqa catqtqctqq acnctqtcca tqaaqcactq aqcaqaaqct ggagqcacaa 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggccnctgcn ccccagcatg gatgacagag tgaaactcca 480
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tcttaaaaaa aaaaaaaaa a
                                                                    501
<210> 452
<211> 51
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(51)
<223> n = A,T,C or G
<400> 452
agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c
                                                                    51
<210> 453
<211> 317
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1) ... (317)
\langle 223 \rangle n = A,T,C or G
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acatetgaag agetagteta teageatetg geaagtgaat tggatggtte teagaaceat 120
ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
tacccatgtc tttatta
<210> 454
<211> 231
<212> DNA
<213> Homo sapiens
<400> 454
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taaqccacqc cacqctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
agaagaccaa attottotgo atoccagott goaaacaaaa ttgttottot aggtotocac 180
ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t
<210> 455
<211> 231
<212> DNA
<213> Homo sapiens
<400> 455
taccaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agctcacaat acagggctcc tttctcctct a
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<210> 456
<211> 231
<212> DNA
<213> Homo sapiens
<400> 456
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tgcactcaaa ttcctttatc aggaataact acatagccac tatttacaaa gccattqqaa 180
cctttttatt tggtgcagct gctagtcagt ccctgactga cattgccaag t
<210> 457
<211> 231
<212> DNA
<213> Homo sapiens
<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A, T, C \text{ or } G
<400> 457
cgaggtaccc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttqttcatca 60
gcattcctta atatgatctt gctataatta gatttttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggcttttgt g
<210> 458
<211> 231
<212> DNA
<213> Homo sapiens
<400> 458
aggtctggtt ccccccactt ccactcccct ctactctctc taggactggg ctgggccaag 60
agaagagggg tggttaggga agccgttgag acctgaagcc ccaccctcta ccttccttca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt ggggggccag accccaggag aagaagattc t
<210> 459
<211> 231
<212> DNA
<213> Homo sapiens
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ccttcgcgaa acctgtggtg gcccaccagt cctaacggga caggacagag agacagagca 120
gccctgcact gttttccctc caccacagec atcctgtccc tcattqqctc tqtqctttcc 180
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<210> 460
<211> 231
<212> DNA
<213> Homo sapiens
<400> 460
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cceactccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180
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<212> DNA
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<210> 462
<211> 231
<212> DNA
<213> Homo sapiens
<400> 462
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qaaqaactqt taqaqaqacc aacagggtag tgggttagag atttccagag tcttacattt 180
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<211> 231
<212> DNA
<213> Homo sapiens
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<210> 464
<211> 231
<212> DNA
<213> Homo sapiens
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aaggacatca catatgaaga atgtttaagt tggaggtggc aacgtgaatt gcaaacaggg 120
cetqettcaq tqactqtqtq cetqtaqtee caqetacteq qqaqtetqtq tqaggecaqq 180
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<211> 231
<212> DNA
<213> Homo sapiens
<400> 465
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gtggcaaatt agcaacaaat tetgacatea tatttatggt ttetgtatet ttgttqatqa 120
aggatggcac aattittigct tgtgttcata atatactcag attaqttcaq ctccatcaga 180
taaactggag acatgcagga cattagggta gtgttgtagc tctggtaatg a
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<211> 231
<212> DNA
<213> Homo sapiens
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cctgtgcaat caaatattgt ggagaattcc ctagctggag aagtcacaaa gactataggc 180
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<212> DNA
<213> Homo sapiens
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tgtgccttaa cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180
gcatgggtct ctgcccaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240
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                                                                311
<210> 468
<211> 3112
<212> DNA
<213> Homo sapiens
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aagatctgca tggtgggaag gacctgatga tacagagttt gataggagac aattaaaggc 120
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aaatgggata cacagtatga tctataaagt gggatatagt atgatctact tcactgqqtt 420
atttgaagga tgaattgaga taatttattt caggtgccta gaacaatgcc cagattagta 480
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gattateatt caateteata gttttgteat ggeecaattt ateeteaett gtgeeteaac 600
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